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FREDERIC MOIR HANES

Late Florence McAlister Professor of Medicine
Duke University School of Medicine

HARVIE BRANSCOMB, Ph.D., *Dean*
DUKE UNIVERSITY DIVINITY SCHOOL

No one of us who has known Dr. Frederic M. Hanes would want to undertake at this hour to state what he meant to us and to this community. We cannot, however, refrain from giving some expression to our sense of gratitude that we were his colleagues, his students, his friends.

He was a scientist. He secured the best training which two continents afforded. He held appointments of distinction in the field of medicine, and was associated with some of the great medical figures of all time. This training and skill he devoted to his native state, first in the city of his birth, then as the administrative head and virtual organizer of the Department of Medicine in this medical school and hospital. He made many contributions to the progress of medicine, publishing numerous valuable articles in scientific journals, and stimulating, directing, and aiding research in his own department and throughout the university. In addition, he was a teacher and a physician. To his students he taught sound and tested principles of medical practice and much besides—the wisdom which came from his broad experience, and the ideals which came from his own character. To his patients he gave himself with that unsparing alertness characteristic of the medical profession at its best.

He was ever responsive to the claims of public service. When the first world war came, he resigned his practice at home, placed himself at the disposition of the government, and served in charge of Base Hospital 65 in France. He accepted positions on state boards and in the work of national philanthropic agencies of many sorts at great expense of time and strength. His services in this area of public life and responsibility were too numerous and too varied ever to be listed or described.

These things are a proud memory to us who knew him, but they are probably not the things which stand out most in our minds today. He was distinguished in the art of medicine, but he excelled also in a much more difficult art, the art of living. The art of living rests upon two principles—a faith in life and a knowledge of and willingness to respond to true values. Dr. Hanes had faith in life. He loved it in all its forms, and his interests were almost limitless. He had learned to know and choose the true values. He chose the arduous activity of the scientist instead of the leisure which was available to him, the enjoyment and creation of beauty rather than the pursuit of ambition, the service of society instead of escape from obligation. He loved much, and he gave of himself and his means to the things which he loved. Thus his many-sided personality has impressed itself upon our institutions, even upon our landscape, but most of all upon our hearts.

There is a phrase in the Old Testament which has repeatedly come into my mind in these last two days. "In those days," says the Scripture, speaking of the possession of

Read in Memorial Services for Dr. Frederic Moir Hanes in the Duke Chapel, March 26, 1946.

the land of Canaan, "there were giants in the land." If we so live that those who come after us will inhabit a new and lovelier Canaan, I do not doubt that when they reflect upon those who did most to make their land so fair and good, and recall the deeds and character of Dr. Hanes, they will say to their children, "In those days there were, indeed, giants in the land."

THE DIAGNOSIS AND MANAGEMENT OF TINEA CAPITIS

J. LAMAR CALLAWAY, M.D.
and
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DURHAM

The problem of epidemic tinea capitis—ringworm of the scalp—among school children of large urban centers has caused much concern in the past few years. An increasing number of cases reported between 1940 and 1945 from the northeastern states—New York[1], Maryland[2], and Pennsylvania[3]—and from Michigan[4] has served to emphasize the infectiousness of tinea capitis and the importance of this disease from a public health standpoint. Because these epidemics have been caused predominantly by infection with Microsporum audouini, the human pathogenic fungus which does not respond readily to treatment, the problem of prevention and control has been extremely difficult.

An epidemic of tinea capitis, caused by M. audouini, has been reported recently from the schools of Graham[5]. Isolated cases have been seen from Rocky Mount, Greensboro, and Fayetteville. There is no doubt, therefore, that the infection has become established in North Carolina. Physicians in the state should report known cases and small epidemic foci to the proper health authorities for evaluation, so that immediate attempts at control may be instituted before large numbers of school children become infected.

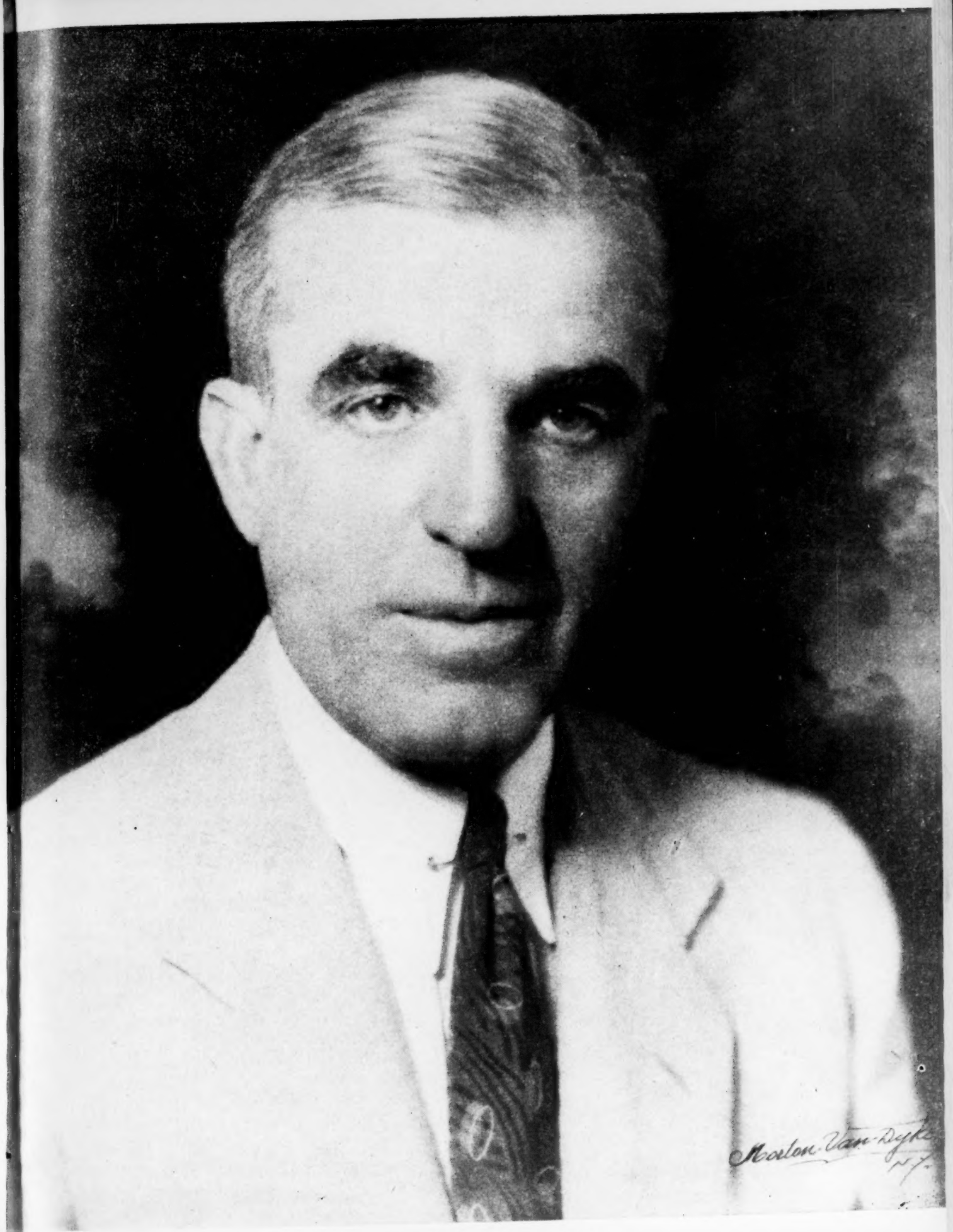
The Medical Problem

Two types of fungi have been responsible for the majority of tinea capitis in this country—namely, M. lanosum and M. audouini. The former is recognized as the so-called animal pathogen, since it commonly causes infection among cats, dogs, horses, and cattle. It occasionally infects human beings who come in contact with such infected animals, causing tinea capitis or tinea corporis in children and only tinea corporis in adults. Control measures should include the treatment of such animal contacts, or provisions for their disposal. Human infections with M. lanosum, however, tend to be sporadic and to heal spontaneously or respond to local treatment over a short period of time.

M. audouini is regarded as a human pathogen, since it cannot be isolated from animals or transferred to laboratory animals by inoculation. This fungus, therefore, spreads from person to person and is the cause of epidemic tinea capitis among children. Infections with M. audouini respond best to x-ray treatment; they heal spontaneously only at puberty, and do not respond readily to local medication. Since x-ray treatment of large numbers of children presents many difficulties, this type of therapy cannot always be used. Unless adequately treated, however, an infected child remains a constant source of infection until he reaches puberty. Because successful treatment requires three to six months in those few cases which do respond to local medication, it is not feasible to remove an infected child from school. Furthermore, such children will act as a focus of infection among the preschool youngsters during the day and will readily come into contact with their schoolmates after the school day is over. An epidemic of tinea capitis caused by M. audouini, therefore, presents a serious public health problem. The infection is maintained by contact from person to person, and treatment is extremely difficult. The treatment period in successful cases extends from three to six

From the Division of Dermatology and Syphilology of the Department of Medicine and from the Division of Bacteriology and Mycology, Duke University School of Medicine.

1. (a) Lewis, G. M., et al.: Measures to Prevent and Control an Epidemic of Ringworm of the Scalp. New York J. Med. 44:1327-1333 (June 15) 1944.
(b) Miller, J. L., Lowenfish, F. P. and Beattie, G. F.: Local Treatment of Tinea Capitis, J.A.M.A. 132:67-70 (Sept. 14) 1946.
(c) Lewis, G. M., Hopper, M. E., and Reiss, F.: Ringworm of the Scalp, J.A.M.A. 132:62-65 (Sept. 14) 1946.
2. Schwartz, L., Peck, S. M., Botvinick, I., and Leibovitz, A. L.: Control of Ringworm of the Scalp among School Children in Hagerstown, Maryland, 1944-1945, J.A.M.A. 132:58-62 (Sept. 14) 1946.
3. Livingood, C. S. and Pillsbury, D. M.: Ringworm of the Scalp, J. Invest. Dermat. 4:43-57 (Feb.) 1941.
4. (a) Burket, L. V.: Present Status of Ringworm Epidermis, Bull. Genessee County M. Soc. (Michigan) 17: 6 (June 23) 1945.
(b) Carrick, L.: The Epidemiology of Tinea Capitis in Detroit School Children, J. Michigan M. Soc. 45:347-352 (March) 1946.
5. Dr. Mildred Morehead of the United States Public Health Service and Dr. J. Roy Hege of the North Carolina State Board of Health are working with the physicians and the local health department in the control of this epidemic.



FREDERIC MOIR HANES, M.D.

September 18, 1883 — March 25, 1946

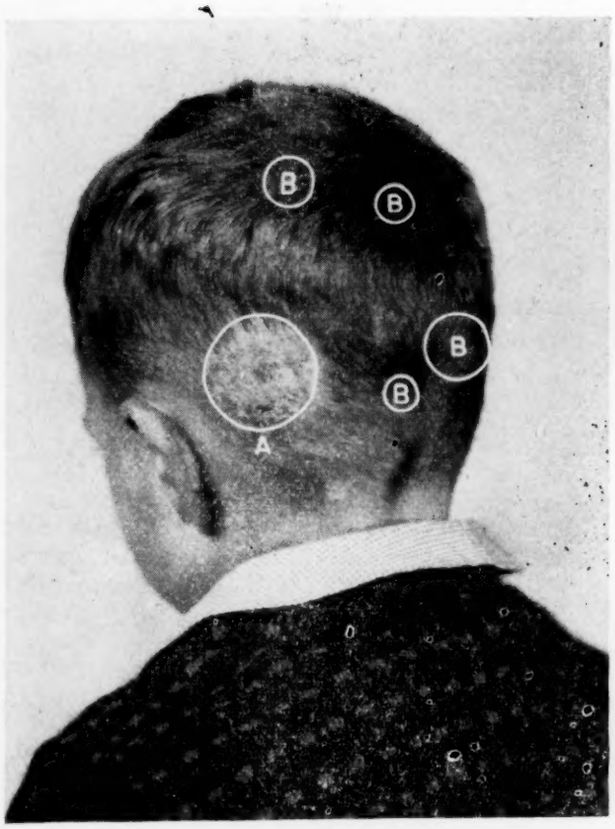


Fig. 1. Photograph of patient with tinea capitis. Area "A" shows clinical involvement and is fluorescent under Wood's light. Areas "B" show no clinical involvement but show brilliant fluorescence under Wood's light.

months, but may continue in some cases until the age of puberty.

Diagnosis

There is no greater aid in the diagnosis of tinea capitis than the Wood's light[6]. Infected hairs fluoresce when exposed to this light in a semi-dark room. The entire scalp should be examined carefully for fluorescent areas which denote infection. An occasional patient may show fluorescence of the eyelashes. In boys the infection is usually seen at the hair line (fig. 1), while girls are more frequently infected at the vertex. Scattered areas of infection may be present in both sexes, however, and an occasional child will show infection of the entire scalp. This method of examination not only allows an accurate determination of the extent of infection on the scalp, but also permits the examiner to detect a minimal infection which might pass ordinary inspection. Several children can be examined in a short period of time, and those showing fluorescent areas should be separated for further examination. Occasionally patients who are under treatment may not show fluorescent areas, even though they are still infected.

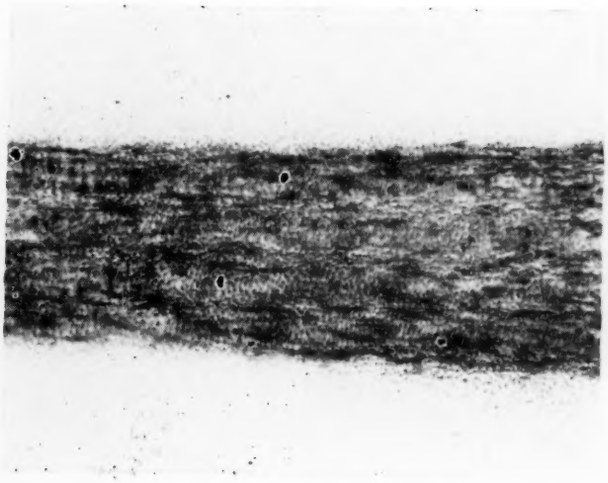


Fig. 2. Photomicrograph of hair, showing organisms in the sheath.

Hairs from areas which fluoresce or from patients suspected of having infection even though they show no fluorescent areas should be epilated and examined microscopically in a 10 per cent potassium hydroxide preparation[8]. Infected hairs are seen to have a spore sheath surrounding the hair shaft and extending from the bulb for a short distance along the hair. The spores are about 1 micron in diameter and are crushed together in the sheath to form a mosaic pattern characteristic of infection by a microsporum (fig. 2). It is not possible to tell, however, which species of microsporum is causing the infection, since the microscopic appearance of the hair is the same regardless of the invading species.

Specific determination of the infecting organism is possible only by culturing infected hairs on Sabouraud's medium and noting the type of colony and spore forms produced. M. lanosum grows quickly, developing a white, cottony, aerial mycelium which becomes somewhat powdery and light brown in the center (fig. 3). When it is examined microscopically, numerous large, spindle-shaped spores are seen (fig. 4). M. audouini grows slowly, producing a matted, wooly colony with radiating furrows (fig. 5). Microscopically the large spores characteristic

6. A simple Wood's light may be constructed by following the outline given in Lewis and Hopper's book(7), or a commercial Wood's light may be purchased from the Strobelite Company, New York, the Westinghouse Electric and Manufacturing Company, Long Island City, New York, Blaklite Products, Chicago, Aloe and Company, St. Louis, and other sources.

7. Lewis, G. M. and Hopper, M. E.: An Introduction to Medical Mycology, ed. 2, Chicago, Year Book Publishers, Inc., 1943.

8. Conant, N. F., et al.: Manual of Clinical Mycology, Philadelphia, W. B. Saunders, 1944.

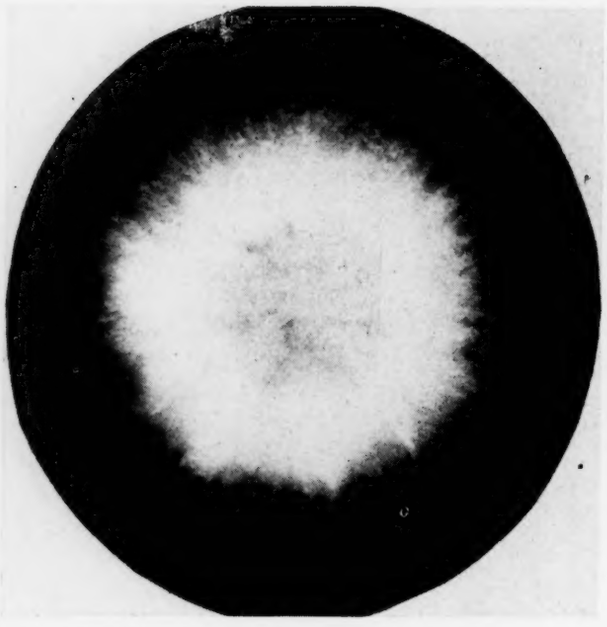


Fig. 3. Culture of Microsporum lanosum.

of M. lanosum are lacking, or are few and poorly formed. Identification of M. audouini is based usually on the type of colony growth and on the presence of raquette mycelium, pectinate hyphae, and nodular bodies seen in microscopic preparations.

Tinea capitis usually occurs in childhood and is rarely, if ever, found after puberty. The earliest lesion usually is seen as a small, scaling, erythematous papule perforated by a hair. Such papules spread peripherally to form patches. The hair becomes lusterless and brittle, breaks off easily, and becomes loosened so that it may be epilated readily. Alopecia usually develops in the infected areas. Since tinea capitis is very contagious, any scaling alopecia occurring in a child should be considered to be tinea capitis until proved otherwise.

Spread of Infection

The most common modes of spread are by way of barber shops, motion picture theaters, schools, playgrounds, and homes. It has been demonstrated that combs, brushes, clippers, and scissors in barber shops sometimes contain infected hairs. Likewise, some theater seats have been found to contain infected hairs. When children play in schools and on playgrounds, they frequently wrestle together and wear one another's caps. At home an infected child may use the comb, brush, and hat of a non-infected child, or may sleep with him. Since there are so many possibilities for spreading infection in an epidemic

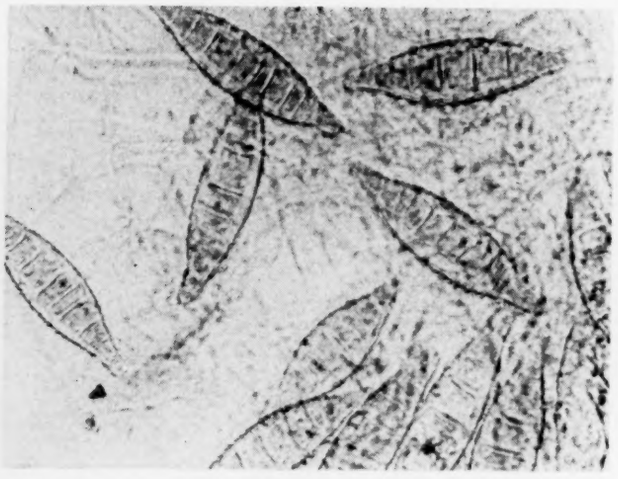


Fig. 4. Photomicrograph of large spores of Microsporum lanosum

of this kind, adequate control measures must be instituted at once and maintained over a long period of time.

Treatment

At the outset it should be stated that if the infecting organism is M. audouini, x-ray epilation of the scalp will almost certainly be necessary. However, some reports on the use of local medication[2,3] are so promising that a trial treatment period is indicated. The following instructions may be given to each patient:

(1) Clip the hair as short as possible with scissors for at least 1 cm. surrounding the affected area as demonstrated by the Wood's light. Burn all clippings. The infected area may be delineated by painting around the infection with gentian violet or other suitable dye.
(2) Wash the scalp once daily with soap and hot water.
(3) Pluck all hairs in the involved area, daily.
(4) Apply the medication daily to all diseased areas, extending at least 1 cm. beyond each infected area. Once a week apply the medicament to the entire scalp.
(5) Wear a tight-fitting skull cap at all times, day and night, to prevent loosened infected hairs from coming in contact with other children. Wear a fresh cap daily. Boil the used skull cap for at least five minutes.
(6) Once a week wash the scalp with soap and water and apply no medication until the patient is examined clinically and under the Wood's light for evidence of activity.

Medications used

Medications used in the treatment of tinea capitis are legion. Schwartz and his co-workers[2] have found the following preparations most effective for local use:

(1) salicylanilide ointment
(2) copper undecylenate ointment
(3) pentachlorphenol ointment
(4) copper oleate ointment
(5) camphor phenol

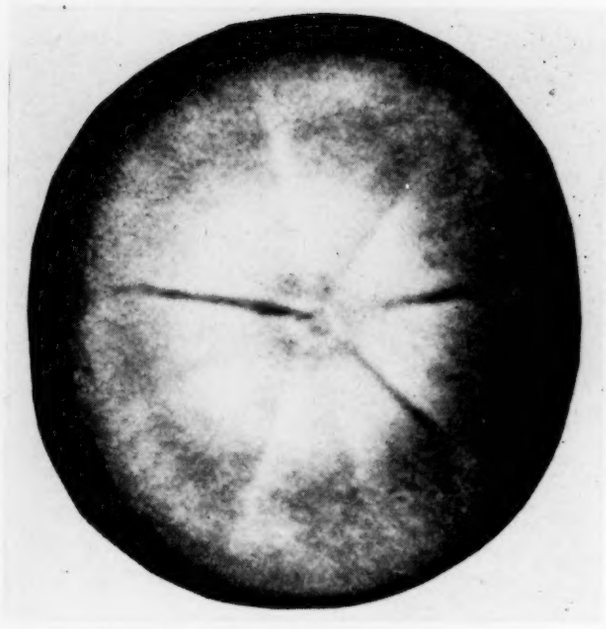


Fig. 5. Culture of Microsporum audouini.

Sodium propionate lotion, sodium propionate ointment, 5 per cent iodine ointment, 5 per cent ammoniated mercury ointment, and pragmatar ointment are other local preparations which may be extremely helpful in local management. The use of estrogenic hormone preparations locally, by mouth, or parenterally is to be condemned.

Miller and his associates[1b] feel that the success of local treatment depends more on the thoroughness of manual epilation than on the fungicide used.

X-ray epilation

If the infection has been proven to be caused by M. audouini, local treatment using one of the medications listed above according to the treatment regimen outlined should be carried out for two to three months. If at the end of that time there is no satisfactory improvement, x-ray epilation is indicated. Unfiltered x-ray therapy (300 r) through five portals according to the McKee technique should be given by a dermatologist or an expert roentgenologist. Roentgen therapy should be followed by manual epilation of any residual hairs, daily shampooing, and the application of medication according to the regimen used prior to x-ray treatment.

Conclusion

Tinea capitis has already become a major public health problem in this state. It has appeared in epidemic form in the schools of Graham, and isolated cases have been seen in patients scattered all over the state. Any child showing alopecia or an inflammatory condition involving the scalp should be examined with the Wood's light and have microscopic examinations made of hairs from the involved area, and cultures for fungi. Isolation techniques and a therapeutic regimen similar to the one outlined should be instituted immediately. A survey should be made of children in the area to see if the infection is wide spread.

THE MANAGEMENT OF MYOCARDIAL INFARCTION

CHRISTOPHER JOHNSTON, M.D.

DURHAM

The patient with a myocardial infarction so massive that death occurs within a few days in spite of all treatment need not be considered here, nor need we consider the unusual patient who has symptoms so mild that the evidence of infarction is picked up many months later by electrocardiographic tracing. There is, however, a large group of patients with moderate to severe symptoms whose recovery depends upon the treatment and clinical judgment of the physician in attendance. Because of the wide variation in the severity of the condition, no set routine of therapy can be followed. Each patient must be treated as an individual.

Management during the Critical Period

Once the diagnosis of myocardial infarction is established, the one rule which seems safest to follow is to consider the patient in critical condition for a period of at least two weeks, no matter how mild the symptoms or signs may be. It is within this period that sudden death is most likely to follow from one of the complications, and it is best to caution members of the family of this possibility. Too much emphasis cannot be placed upon the psychologic management of the patient himself, however; usually he is already in fear of death, and any sign of anxiety in the physician or family will serve to terrorize him further. Such a statement should be superfluous; yet it is astonishing how freqently the physician himself is responsible for increasing the apprehension of the patient.

From the Department of Medicine, Duke University School of Medicine, and Duke Hospital, Durham, North Carolina.

Rest

Bed rest is obviously necessary in the treatment of any patient with myocardial infarction. It is generally thought that four weeks is the minimum time required for the healing of even a small infarct, and that six weeks should be allowed for healing if it is thought that the infarction is reasonably large. After this period of time bed rest is not indicated save in the few patients actually in congestive failure.

Much discussion has arisen over the question as to whether or not the use of a bed pan is essential during the period of strict bed rest. At present the prevailing opinion is that, if the patient can use the pan without discomfort, he should do so; but that when the use of the bedpan becomes an ordeal and leaves the patient exhausted there may be actually less strain upon the myocardium if the patient is assisted to a bedside commode.

The use of the telephone for business calls should be rigidly prohibited, and ordinarily the patient should not use the telephone at all, except occasionally when a call from one of the family may be reassuring to him. Visitors should be excluded, except for members of the immediate family and close personal friends, and even these visits should be restricted to a few minutes. Good nursing care is essential in order to help the patient to carry out the restrictions. Members of the family may help as necessary, but should be under the direction of a competent nurse at all times.

The diet depends on the patient's condition. Usually during the first few critical days the food intake is restricted to fruit juices and milk. This diet may be prolonged through the first week, but usually during the second and succeeding weeks the patient is able to take a light diet. The important rules to follow are that the food be easily digestible and that the patient never overeat at any one meal. It is important to give the patient enough fluids, for in the few days following relatively extensive myocardial infarction there is more danger of his becoming dehydrated than of receiving too much fluid.

Medication

Some opiate is indicated in nearly every case of myocardial infarction, not alone for the relief of pain but also for its effect in producing a certain amount of euphoria, or at least some relief from the feeling of apprehension. Pantopon can be substituted for morphine; often dilaudid is preferable to any other opiate because it so rarely causes nausea and vomiting. No definite rule can be given for the dosage of any of these drugs. If comparatively large doses fail to relieve the pain, the administration of massive doses is contraindicated; they seldom relieve the pain, and usually add to the anoxemia by depression of the respiratory center. The pain in coronary occlusion rarely persists more than two or three days, and after this period the opiates are generally of little value unless the patient is suffering from congestive failure and dyspnea which are not relieved by other medications. Demerol has not yet been used sufficiently to show its value in the acute stage of infarction, but should be tried where possible. It provides fairly effective relief of pain without depression of the respiratory center.

The more rapidly acting coronary dilators such as amyl nitrite are contraindicated; they not only fail to relieve pain and the local ischemia, but they serve further to reduce blood pressure, which often is dangerously lowered. There is evidence to show that after the patient has recovered from the acute shock of the occlusion, however, aminophyllin may favor the development of a collateral circulation and decrease the area of infarction. At present clinical evidence would seem also to favor the use of papaverine, which is devoid of all narcotic effect, but does cause dilatation of the coronary vessels. Aminophyllin is given preferably in the enteric-coated tablets in doses of 0.2 Gm. three or four times daily, and papaverine by hypodermic in doses of 64 mg. every four hours.

Glucose is of especial benefit during the first twenty-four or forty-eight hours after the onset of the attack. Not only does the patient's general condition improve, but often surprising relief from the pain is obtained. Some writers advocate the intravenous injection of 50 cc. of a 50 per cent solution of glucose by syringe, but it would seem better to give 100 cc. of 25 per cent glucose by slow intravenous drip. If there are evidences of much dehydration as a result of the profuse perspiration accompanying an infarction, larger doses of more dilute glucose may be used without danger, provided the drip is given slowly.

Digitalis is contraindicated. If the heart should respond with increased strength of contraction, the danger of rupture or aneurysm formation in the area of the softened muscle is increased. Furthermore, the action of digitalis in increasing cardiac irritability might lead to the development of serious arrhythmia. Later on, however, when healing is complete or nearly complete and when there is evidence of considerable decrease in cardiac reserve or of actual congestive failure, digitalis may be used without fear and with distinctly beneficial results. Quinidine at one time was employed frequently, and by some physicians routinely, in an effort to prevent the onset of ventricular tachycardia. In more recent years, however, its use has been restricted, and at present is usually limited to those patients showing numerous premature contractions as an evidence of increased ventricular irritability. Even in these cases it should be used with considerable caution and in doses not exceeding 0.2 to 0.4 Gm. every four hours day and night. There is evidence to show that atropine may help in the prevention of abnormal rhythms, and during the acute stages following infarction it may be used together with morphine. Large doses are contraindicated, however—both because of the resultant tachycardia, and because the dryness of the mouth makes the patient most uncomfortable, especially if fluids are restricted because of evidence of congestive failure.

Oxygen is of considerable benefit, especially in the patient who is cyanotic and in respiratory distress. Many patients are more comfortable psychologically when receiving oxygen by nasal catheter or in the oxygen tent, and become apprehensive when oxygen is discontinued. In such cases it is well to leave an oxygen tank at the bedside, as its presence seems reassuring to the patient. Other patients, however, react quite unfavorably to the use of oxygen, struggle against the nasal catheter, and feel apprehensive when placed in the tent. In such patients the restlessness and apprehension usually more than offset the benefit obtained by the use of oxygen.

In many patients following myocardial infarction the systolic blood pressure goes so low as to prevent glomerular filtration, and anuria results. The physician must differentiate between anuria and retention, so as to avoid catheterization when it is not indicated. Since the anuria is simply the result of a lowered blood pressure, diuretics will do no good during the acute failure. After the pressure has risen to normal, however, mercurial diuretics may be indicated if there is evidence of congestive failure. Often when the patient is not progressing well it is surprising how much diuresis can be obtained when there is no demonstrable pitting edema or obvious rales in the lung bases. Patients with congestive failure usually have albuminuria as a result of chronic passive congestion of the kidneys. This finding in itself is no contraindication to the use of the mercurial diuretics which, if necessary, may be repeated every two or three days. If satisfactory diuresis is not obtained by the mercurial diuretic alone, it is well to prepare the patient by giving 10 Gm. of ammonium chloride (usually 2 Gm. five times daily) for two days, and to administer the diuretic on the morning of the second day. Large doses of ammonium chloride often cause nausea and vomiting, and should not be given if good results can be obtained from the mercurial diuretic alone.

Emergency stimulants such as metrazol or coramine, although they are at times life saving, should be used with extreme caution, for the primary objective in the treatment of coronary occlusion is to give the weakened myocardium as much rest as possible. It is generally true that when such stimulants are needed at frequent intervals the area of infarction is so large as to make the prognosis hopeless. Mention should perhaps be made here of the use of caffeine. When the patient is able to take nourishment and is accustomed to a morning cup of coffee, there is no contraindication to its use; indeed, its mild diuretic action may be beneficial.

Mild sedation is indicated in nearly every case of myocardial infarction, especially in the aggressive, restless type of patient who rebels under the necessary restraint. Phenobarbital in doses of 30 mg. two or three times daily is helpful, but patients may complain that it makes them mentally sluggish. In such cases mebaral in doses of 0.1 Gm. two or three times daily should be given, as it causes mental relaxation without inducing a feeling of sluggishness. The dangers of overdosage are not great with either of these sedatives, and should symptoms of overdosage arise, they will subside promptly upon withdrawal of the drug. Bromides should

be used with caution, especially since the salt intake is generally low and even therapeutic doses of the bromides may cause intoxication which may take several days to wear off. At bedtime some hypnotic may be necessary, and a wide variety of these medications are available.

The matter of elimination is often of more concern to the patient and the family than to the physician, who knows it is better for the patient to go four or five days without a bowel movement than to be worn out by the excessive use of laxatives or enemas. Sooner or later, however, some aid to elimination is necessary in practically all patients. Although the patient should not be permitted to dictate the medication he is to receive, it is often well to find out what laxatives have worked well in the past without causing excessive pain or discomfort. Some patients take enemas easily, in which case the water and glycerine enema is perhaps preferable to all others. If the patient reacts poorly to enemas, however, the use of a saline laxative is preferable. One should bear in mind that after four or five days fecal impaction may be present, and if the enema returns clear or if the laxative is ineffectual rectal examination is indicated immediately.

Since nearly every case of myocardial infarction is on the basis of coronary thrombosis, it would seem reasonable to use some anticoagulant to prevent further propagation of the clot to involve another branch of the coronary vessels. As yet, however, it seems imperative to restrict the use of dicumarol or heparin to patients who are in hospitals where daily determinations of the prothrombin time may be made. These preparations seem to offer great promise in the future, but overenthusiastic use without proper control is obviously unwise.

Management during Convalescence

When the patient has passed the acute period of danger and is well on the way to recovery, it is well to explain to him why it is necessary to remain in bed for a further period of time in order to obtain good healing of the infarction. This explanation can be made without frightening the patient, and once he understands the need for the prolonged period of bed rest he will cooperate. The patient who is put off from day to day with vague promises will soon feel that the truth is being withheld, and will either become more and more apprehensive, or will conclude that the physician is an alarmist and will accordingly disregard his orders.

Throughout the period of convalescence some of the restrictions imposed during the first two weeks may be relaxed, and the patient may be allowed to have a few visitors each day, depending upon his condition. It is strange how otherwise intelligent people become insulted when refused admission to the room of a patient who has already seen his quota of visitors for the day. The one practical solution to this problem is to keep a daily list of visitors and, if necessary, make appointments in advance.

During the last week of absolute bed rest it is well to give light massage to the arms and legs to restore some measure of tone to the muscles, which have grown flabby through disuse. Active and passive movements of the extremities at various times during the day are also in order, provided the patient is in condition to carry them out.

When at long last the bed rest has terminated, it is time to start the patient on graduated exercises. These at the start may consist of nothing more than five minutes on the side of the bed, with the feet in a chair. The period should be extended gradually each day, depending upon the patient's response and general gain of strength. After he can sit up for thirty minutes, it is time to have him sit in a chair at the bedside. Obviously sitting in a chair is easier than sitting on the side of the bed, but at the start it is well to have the patient in bed, so that if he feels weak or dizzy he has merely to lie back in the bed. When he is able to sit up as much as thirty minutes in a chair, he should be allowed to sit up for this length of time twice daily. Each of these periods may be extended daily by fifteen to thirty minutes, depending entirely upon the patient's response. After a few days, he should start walking around the room.

Management after Recovery

Finally the patient should venture outdoors for short walks gradually lengthened. Too much emphasis cannot be placed upon the fact that the only restriction ultimately will be the amount of exercise the patient finds he can take without substernal pain, oppression, shortness of breath, or other evidences of having exceeded the cardiac reserve. Only too often these patients are

threatened with dire consequences if they walk more than short distances, whereas many of them actually can, by gradually increasing the walk, work up to five miles at a time. There is nothing quite so reassuring to the patient as the knowledge that he can live normally again. On the other hand, if the patient has to stop for breath every time he tries to go more than a short distance, it is unwise to try to push him beyond the limits of his cardiac reserve.

Many patients who have had coronary occlusions ultimately return to their work and recreation and live just as they did before; there is no reason to think that the patient will suffer any harm, provided he lives within the limits of his cardiac reserve.

THE TREATMENT OF CONGESTIVE HEART FAILURE

EDWARD S. ORGAIN, M.D.

DURHAM

The term "heart failure" implies the inability of the heart to maintain an output of blood adequate for body needs under conditions both routine and emergent. While two primary types of heart failure may be distinguished[1]—"forward failure" and "backward failure"—, features of both commonly coexist in either situation. The present paper will consider only the treatment of the second type—that is, congestive heart failure. This is the more frequent form, in which cardiac enlargement and congestion of the various body tissues predominate.

The management of congestive heart failure depends to a large extent upon the symptoms and signs indicating the cause and degree of failure. Each program of therapy must be individualized to meet the patient's particular needs. In general, however, therapeutic measures are directed toward reducing the work load upon the heart by rest, increasing its mechanical efficiency as a pump by digitalis, decreasing salt retention by diet, and promoting fluid excretion by diuretics. In the majority of instances a few simple rules are accepted.

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1. (a) Harrison, T. R.: Failure of the Circulation, ed. 2, Baltimore, Williams and Wilkins Company, 1939.
   (b) Boyer, N. H.: Cardiogenic Shock, New England J. Med. 230:226-229 (Feb. 24); 256-260 (March 2) 1944.
   (c) Ellis, L. B.: The Mechanism of Heart Failure and Related States, New England J. Med. 228:284-288 (March 4); 311-313 (March 11) 1943.

Rest

Physical rest, until compensation has been fully restored, is mandatory in order to reduce the demands for blood upon the already overburdened heart. Rest may be obtained in a comfortable bed with the head elevated, or in a large easy chair provided with arm rests. Rigid bed rest is not imperative and may be harmful, particularly if it is prolonged in elderly patients.

The judicious use of sedatives in the form of hypnotics (barbiturates) or narcotics (codeine, morphine, or dilaudid) promotes rest, relaxation, and sleep, and in addition, decreases dyspnea and cough. Narcotics, however, predispose to the development of Cheyne-Stokes respiration in the hypertensive and arteriosclerotic subject.

Diet and Fluid Intake

Recent acquisitions to our knowledge concerning fluid dynamics in congestive heart failure[2] have served to reorient former opinions regarding diet and fluid intake[3]. In the patient exhibiting edema, the most important part of the dietary regimen is restriction of sodium intake, for an excess of the sodium salt leads to fluid retention. When sodium in the diet is maintained at low levels, fluid restriction becomes unnecessary, for large amounts of fluid are well tolerated by the patient[4]. When fluids are restricted below 1500 cc. per day, thirst is common. By contrast, when fluids are forced beyond 3000 cc. orally, abdominal discomfort is frequent. The most sensible program would seem to be to allow the patient fluids in accordance with his own desires. It may be necessary to urge certain individuals to take 2000 to 2500 cc. of fluid per day in order to insure adequate urinary excretion. The average diet contains 4 to 12 Gm. of sodium chloride, but diets very low in sodium may be attained simply by proper selection of foods, the use of salt-free bread and butter, and the omission of salt in cooking. The restriction of sodium to levels of .5 to 1 Gm. per day may achieve brilliant results in patients with chronic and recurrent heart failure.

2. Warren, J. V. and Stead, E. A., Jr.: Fluid Dynamics in Chronic Congestive Heart Failure, Arch. Int. Med. 73:138-147 (Feb.) 1944.
3. (a) Wheeler, E. O., Bridges, W. C., and White, P. D.: Diet Low in Salt (Sodium) in Congestive Heart Failure, J.A.M.A. 133:16-20 (Jan. 4) 1947.
   (b) Leevy, C. M., Strazza, J. A., and Jaffin, A. E.: Fluids in Congestive Heart Failure, J.A.M.A. 131:1120-1125 (Aug. 3) 1946.
4. Schroeder, H. A.: Studies on Congestive Heart Failure. I. The Importance of Restriction of Salt as Compared to Water, Am. Heart J. 22:141-153 (Aug.) 1941.

Initially, an adequate caloric intake is relatively unimportant. The diet should be light, nutritious, and high in carbohydrates, but low in salt content. The modified Karell diet[5] or the ordinary cardiac "soft" diet, with four to six feedings per day, is satisfactory. As the patient improves, a gradual shift may be made to a bland diet low in total sodium. Because protein and vitamin deficiencies are likely to occur in the chronic cardiac patient with longstanding and recurrent failure, these deficiencies must be corrected. The protein intake should range between 50 and 70 Gm. per day. Since a manifest single vitamin deficiency is uncommon, the diet should be supplemented with one of the multi-vitamin preparations, given either orally or parenterally.

A new approach[6] to the therapy of heart failure employs a neutral or slightly acid ash diet containing 0.85 Gm. of sodium supplemented by hydrochloric acid and ammonium chloride orally for purposes of acidification. The rationale is based upon the theory that the excretion of sodium is favored by the acidifying program. In addition, fluids are forced to levels varying from 3000 cc. to 8000 cc. per day, by both oral and parenteral routes, in order to combat thirst and dehydration and to promote diuresis. This regimen has not been accepted generally, except in modified form.

Diuretics

Diuretics are useful adjuvants to therapy. By promoting the excretion of fluid by the kidney, they reduce the blood volume, venous pressure, and tissue edema. The xanthine diuretics presumably act by increasing renal blood flow and renal filtration. The oral preparations of this group consist principally of theophylline and theobromine and their related salts. Theophylline and its derivatives are more effective than the theobromines, but tend to evoke nausea and vomiting more easily. These drugs should be administered in the maximum tolerated dosage, preferably divided equally in three or four doses a day to avoid gastric irritation. The average range of daily dosage which is usually well tolerated is as follows: theophylline, 0.6 to 0.9 Gm.; theophylline sodium acetate, 1 to 2 Gm.; theophylline ethylenediamine (aminophyllin), 0.3 to 0.6 Gm. (enteric coated); theophylline calcium salicylate (phyllicin), 0.6 to 0.9 Gm.; theobromine, 0.9 to 1.8 Gm.; theobromine sodium salicylate (diuretin), 2.6 to 4 Gm.; theobromine calcium salicylate (theocalcin), 1.5 to 3 Gm.; and theobromine sodium acetate, 1.5 to 3 Gm. Less nausea and vomiting result, and probably equal therapeutic effect is obtained if these drugs are administered for a period of one or two days, then omitted for an equal length of time. Aminophyllin may be given in the form of rectal suppositories (0.25 to 0.5 Gm.) or intravenously (0.24 Gm. in 50 cc. of fluid, 0.48 Gm. in 100 cc. of fluid), both for its diuretic effect and for its bronchodilating action, which relieves dyspnea. Caution must be observed when the drug is given intravenously (always slowly and through a small needle), for in some instances reactions of the collapse type may occur in patients with serious, acute myocardial damage (infarction) or severe congestive heart failure.

The mercurial diuretics unquestionably are the most potent diuretics now available, and they owe their action to a direct effect upon the renal tubules which inhibits the reabsorption of fluid. Probably the best known and most widely used mercurials are salyrgan combined with theophylline, and mercupurin, both of which contain mercury and theophylline. The addition of the xanthine enhances the diuretic effect of the mercurial. The best effects are obtained by the intravenous administration of these drugs, beginning with 0.5 cc. and increasing gradually to a maximum of 2 cc. Subsequent doses may be administered at intervals of two days to a week. Salyrgan and mercupurin produce pain when given intramuscularly, and cause necrosis in the skin and subcutaneous tissues. A new mercurial, mercuhydrin, is suitable for intramuscular injection at similar dosage levels. The urine must be watched carefully for albumin and cellular elements denoting a deleterious effect upon the kidney. The effectiveness of the mercurial drugs may be increased materially by the preliminary administration of such acidifying salts as ammonium chloride or ammonium nitrate, 4 to 6 Gm. daily, given in enteric-coated pills (0.5 Gm.) in divided doses three or four times daily.

5. Bannick, E. G. and Smith, F. H.: The Karell Diet and a Modified Karell Diet in the Treatment of Cardiac Dropsy, J. Am. Dietet. Assoc. 2:246-249 (March) 1927.

6. Schemm, F. R.: A High Fluid Intake in the Management of Edema, Especially Cardiac Edema. I. The Details and Basis of the Regime, Ann. Int. Med. 17:952-969 (Dec.) 1942; II. Clinical Observations and Data, Ann. Int. Med. 21:937-976 (Dec.) 1944.

Digitalis and the Cardiac Glycosides

Digitalis is the most effective single therapeutic agent in the treatment of heart failure. In most instances the oral administration of the whole digitalis leaf (representing a mixture of glycosides) in tablet form is satisfactory, simple, and effective[7]. The average digitalizing dose may be roughly calculated as 0.1 Gm. of digitalis (1 U.S.P. XII unit) for each ten pounds of body weight. Thus, between 1 and 2 Gm. of digitalis (10 to 20 U.S.P. XII units) is necessary for complete digitalization. This amount should be prescribed in divided doses over a period of several days in order to prevent gastrointestinal irritation or the development of rapid intoxication. Digitalis should be continued until some effect, whether therapeutic or toxic, is noted. The rapidity of its administration will vary with the needs of the individual case. Since digitalis is excreted at a rate of approximately 0.1 to 0.15 Gm. per day, this amount should be given as a maintenance dose and continued indefinitely, even after full compensation has been restored. When the oral route is not feasible, digifolin may be used intramuscularly; it should be remembered, however, that only one-third to one-fifth as much in terms of U.S.P. units will be required for parenteral as for oral digitalization.

The most significant advance in digitalis therapy[8] is the recent introduction of the purified principles of digitalis leaf, the cardiac glycosides, to which digitalis leaf preparations owe their action. The most important member of this group is digitoxin, which, assayed gravimetrically, has a potency 1,000 times as great as that of digitalis; for example, 0.1 mg. of digitoxin is equivalent in potency to 0.1 Gm. of digitalis. Digitoxin is unique among the digitalis group, in that it is wholly absorbed when given orally; thus the dose required for complete digitalization is the same, whether the drug be given orally or intravenously[9]. The average digitalizing dose of the drug is 1.2 mg.; this may be administered as a single dose with little evidence of intoxication, but preferably is divided into two equal portions given at six-hour intervals. The maintenance dose is 0.1 to 0.2 mg. daily. Since digitoxin is excreted as slowly as digitalis leaf, a shift from intravenous digitalization to oral maintenance is made without difficulty.

The physician should familiarize himself with two other preparations for even more rapid intravenous digitalization. Ouabain (crystalline G-strophanthin) exerts early effects in ten to twenty minutes; its maximal action is reached in two hours. A safe initial intravenous dose is 0.5 mg., but caution is required for subsequent injections of 0.1 mg. at hourly intervals, never to exceed a total dosage of 0.9 mg. The dosage of lanatosid C, also a useful intravenous preparation, is 1.6 mg. given in two equal parts at intervals of four hours. Because ouabain and lanatosid C are excreted rapidly in forty-eight to seventy-two hours, maintenance doses are judged with difficulty, and a transfer to oral digitalis leaf (or digitoxin) is customary at the end of twenty-four hours. Intravenous digitalization is rarely necessary and should never be proposed for a patient who has received digitalis recently in other forms.

Other Therapeutic Measures

Oxygen inhalation therapy in concentrations of 100 per cent is of value when arterial unsaturation leading to cyanosis is present. It has been recommended, particularly in coronary artery thrombosis, to increase the amount of oxygen available to the myocardium. Stimulants such as caffeine, coramine, and metrazol are of value for the relief of Cheyne-Stokes respiration. The withdrawal of 500 to 700 cc. of blood by venesection is useful when the venous pressure is high.

Paracentesis of the thorax may be performed for relief of dyspnea whenever the amount of fluid to be removed is greater than 500 cc.; abdominal paracentesis may be done whenever it seems probable that 1500 to 2000 cc. of fluid will be withdrawn. However, paracentesis removes body proteins, and if it seems likely that the patient will absorb his own cavity fluid, such loss of protein should be avoided. The use of Southey tubes to drain local tissue edema in the lower extremities or in the scrotum is valuable in some cases, but great care must be exercised, lest the tissue become infected.

Emergency treatment may be necessitated by sudden failure of the left ventricle, which

7. Brome, R. A., Jr. and Orgain, E. S.: The Practical Use of Digitalis, North Carolina M. J. 7:3-8 (Jan.) 1946.
8. (a) Gold, H.: Pharmacologic Basis of Cardiac Therapy, J.A.M.A. 132:547-554 (Nov. 9) 1946.
   (b) Freedberg, A. S. and Zoll, P. M.: Digitalis, New England J. Med. 235:938-945 (Dec. 26) 1946.
   (c) Broome, R. A., Jr. and Orgain, E.S.:The Cardiac Glycosides, North Carolina M. J. 7:61-65 (Feb.) 1946.
9. The cardiac glycosides should not be given subcutaneously or intramuscularly because of local irritation.

produces acute pulmonary edema associated with great anxiety, intense dyspnea, orthopnea, and cardiac asthma. In most instances morphine, 15 mg., combined with atropine, 0.6 mg. subcutaneously, and aminophyllin, 0.24 to 0.48 Gm., given slowly by vein will suffice to abort the attack. However, rapid intravenous digitalization with a cardiac glycoside may be imperative and life saving. The application of cuffs around all four extremities to induce peripheral stasis will delay the venous return of blood to the lungs. If the venous pressure is high, 500 to 700 cc. of blood may be withdrawn rapidly by venesection to decrease pulmonary congestion. The inhalation of oxygen in 100 per cent concentration by tent, mask, or catheter combats anoxemia and relieves dyspnea.

Prophylactic Measures

When the phenomena associated with congestive heart failure have disappeared and compensation has been restored, the patient may be allowed to resume slowly a program of limited activity compatible with an asymptomatic existence. The body weight must be stabilized at normal or substandard levels. Respiratory infections, particularly, should be avoided and treated with unusual care. Recurrent episodes of heart failure can be curtailed effectively by the intelligent use of rest and sedation, a diet low in sodium content, the maintenance of full digitalization, and the frequent administration of diuretics, particularly the mercurials, in order to prevent or to relieve latent fluid retention.

TREATMENT OF CARDIAC FAILURE WITH THE RICE DIET

History of a Patient with Myocardial Aneurysm

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In a large number of patients with kidney disease and hypertensive cardiovascular disease treated with the rice diet, the enlarged heart became smaller, the inverted T_1 became upright, and the signs and symptoms of cardiac failure disappeared[1]. The rice diet has also proved beneficial in patients with cardiac failure due to other causes (aortic and mitral valvular lesions, auricular fibrillation, left bundle branch block, and so forth).

The diet contains in 2000 calories not more than 200 mg. of chloride and 150 mg. of sodium. The daily fluid intake is, in most instances, not more than 800 cc. In patients who have no sodium chloride retention at the beginning of the rice diet and no "renal leakage" of sodium chloride, the urinary chloride concentration after two months on the diet is about 10 mg. per 100 cc., the sodium concentration about 1 mg. per 100 cc.; the sodium-potassium ratio in the urine is about .003 (compared with 2 on a "normal" diet).

The history of a patient with myocardial infarction followed by myocardial aneurysm is given as an example of the effect of the rice diet in cardiac failure.

Case Report

M. C. (B85425), a 45-year-old white county farm agent, was admitted to Duke Hospital August 5, 1946.

History: The patient's father died at 54 of heart trouble; his mother died at 58 of a stroke. The patient's general health had always been very good except for increasing obesity. "Hypertension and overweight" (250 pounds) forced him "to take it easy since the spring of 1944."

In April, 1945, the patient suddenly developed fever and dizziness, and was sent to a hospital. He was unconscious for several hours and "out of his head for some time afterwards." The systolic blood pressure, which according to the patient had been around 200, fell to 140. There was no precordial pain at any time. The fever persisted for two weeks. At discharge, he was advised to rest and to take digitalis.

In June, 1945, the patient developed "fluid in his chest," dyspnea, and orthopnea. The systolic blood pressure was 150. In August, 1945, for two weeks, he was treated in another hospital with oxygen, a low-protein, salt-poor diet, and ammonium chloride. He felt better and was able to be up and about. In November, 1945, albumin (2 to 4 plus) and casts were found in the urine. Ascites and ankle edema began. From January, 1946 on, his condition grew steadily worse, the dyspnea causing the greatest discomfort. For five days in May, 1946, he felt mentally confused. About the same time, he developed

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1. Kempner, W.: (a) Treatment of Kidney Disease and Hypertensive Vascular Disease with Rice Diet, North Carolina M. J. 5:125-133 (April) 1944; (b) Compensation of Renal Metabolic Dysfunction, North Carolina M. J. 6:61-87 (February); 117-161 (March) 1945; (c) Some Effects of the Rice Diet Treatment of Kidney Disease and Hypertension, Bull. New York Acad. Med. 22:358-370 (July) 1946.

a decubitus ulcer over the coccyx. Since June, he had had considerable soreness of the tongue.

He was under medical care during all this time, and between January and July, 1946, he spent one hundred and twenty-six days in three different hospitals. In addition to digitalis for more than a year (1.7 grains of digitora daily since June 15, 1946) and a salt-poor diet, he was given salyrgan (seven injections since May 15, 1946), aminophyllin (twelve injections since May 15, 1946) and glucose intravenously, and ammonium chloride (3 to 6 Gm. daily from August 30, 1945, to May 15, 1946), theominal, coramine, barbital, and other sedatives.

In spite of this treatment, the cardiac failure increased. On July 29, a paracentesis was done and 2 gallons of fluid were removed, but a week later the abdomen was swollen as much as before and the edema had become worse.

Physical examination (August 5, 1946): The patient's weight was 187 pounds, height 5 feet, 10 inches, temperature 37 C. (98.6 F.), pulse 86, respiration 16. His blood pressure during the first week averaged 126 systolic, 88 diastolic. He was a well developed, poorly nourished, white man in considerable respiratory distress. There was generalized anasarca, and the skin was pale. Over the coccyx was a decubitus ulcer measuring approximately 1 inch in diameter. The eyes had a marked stare; the eyegrounds showed only slight tortuosity of the vessels. The tongue was very red, smooth, and sore, and along the lateral margins were several ulcers. There was engorgement of the neck veins, and rales were heard at both lung bases.

The heart was markedly enlarged, chiefly to the left. The maximum apical impulse was in the fifth interspace 14 cm. from the midsternal line. The sounds at the base were forceful, and the second pulmonic sound was louder than the second aortic. The first sound at the apex was weak and was followed by a loud, long, blowing systolic murmur. During the period of this murmur, a high-pitched murmur of shorter duration was heard.

The abdomen was large, round, distended, and filled with fluid. A non-tender liver edge was felt 6 cm. below the costal margin. There was marked sacral and scrotal edema and severe pitting edema of the ankles and legs.

Accessory findings: The chest film showed a slight increase in the markings at both lung bases. The heart appeared enlarged, especially to the left, and there was an area of increased density along the left border of the heart that was thought to be due to a myocardial aneurysm (Dr. J. G. Whildin). Further x-ray studies by fluoroscopy and films (Drs. G. Baylin and R. J. Reeves) confirmed the presence of a myocardial aneurysm of the postero-lateral wall of the left ventricle (fig. 1).

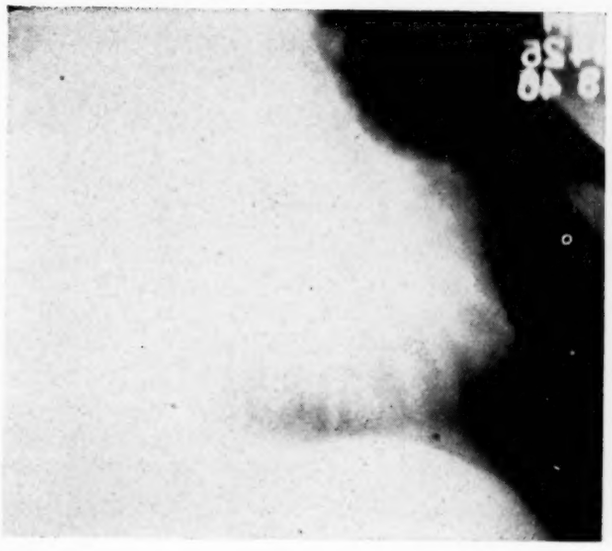

Fig. 1

As is shown in table 1, the electrocardiogram showed right axis deviation; the venous pressure was increased, the renal reserve was diminished, and hypoproteinemia, hypocalcemia, and albuminuria were present.

Impression: Myocardial aneurysm following myocardial infarction. Advanced myocardial failure.

Course: On August 7, the patient was started on a 2600-calorie rice diet with 800 cc. of fruit juices, supplemented by vitamins A, B, C, and D, and ferrous sulfate (0.6 Gm. three times a day). All other medication was discontinued except digitalis (1 cat unit of digifolin daily), and oxygen inhalation.

A paracentesis was done on the ninth hospital day; 8000 cc. of fluid were removed. Four days later, the patient had a chill and fever. The temperature became normal twenty-four hours after treatment with penicillin was started.

The patient ate the diet well; it was increased to 2900 calories on August 30, and to 3100 calories on October 16.

By the end of the fifth week, his weight

Table 1

Accessory Findings

	Aug. 5-12, 1946	Oct. 29-Nov. 18, 1946
Blood pressure (mm. Hg.)	126/88	100/70
Hemoglobin (percent. of 15.5 Gm.)	86	85
Red blood cells	4,200,000	4,400,000
White blood cells	6,100	7,000
Nonprotein nitrogen (mg. per 100 cc. of blood)	32	23
Urea nitrogen (mg. per 100 cc. of blood)	12.9	7.9
Urea ratio (percent.)	40.3	34.3
Sugar (mg. per 100 cc. of blood)	87	
Total proteins (Gm. per 100 cc. of plasma)	5.7	7.1
Globulin (Gm. per 100 cc. of plasma)	2.9	3.4
Albumin (Gm. per 100 cc. of plasma)	2.8	3.7
Albumin-globulin ratio	1.04	0.91
Calcium (mg. per 100 cc. of serum)	7.2	8.5
Phosphorus (mg. per 100 cc. of serum)	3.9	4.2
Cholesterol (mg. per 100 cc. of serum)	160	140(Sept.5)
Chlorides (as mg. NaCl per 100 cc. of plasma)	616	584
Phenolsulfonphthalein (percent. excreted in 2 hours)	41	50
Urea clearance (percent. of normal)	9.9	
Mosenthal (concentration-dilution) test	1.019-1.024	
Urine albumin (Gm. per 1000 cc.)	0.85	0.06
Urine chlorides (as mg. NaCl per 100 cc.)	429	26
Total nitrogen excreted in urine in 24 hours (Gm.)		2.75
Basal metabolic rate (percent.)	+21	+5
Electrocardiogram		
T waves	T_1 isolectric, $T_{2,3}$ flat, T_4 inverted, $ST_{2,3}$ depressed.	$T_{1,2,3}$ more upright. ST_3 depressed. T_4 upright.
Angle of electrical axis (degrees)	+106	+95
Venous pressure (mm. of saline)	185	70 (Oct. 3)
Transverse diameter of heart (cm.)	19.75	17.15
Diameter of great vessels (cm.)	8.85	6.3
Weight (Kg.)	85	64.1
Liver enlargement (cm. below costal margin)	6	0
Circumference of abdomen, at umbilicus (cm.)	110	83
Circumference of each leg, 7 cm. above lateral malleolus (cm.)	25	20.5

had decreased from 85 Kg. (187 pounds) to 67 Kg. (148 pounds). The urine volume was regularly greater than the fluid intake. Most of the edema had disappeared, and the liver was smaller in size. The decubitus ulcer had healed. The total plasma proteins had risen from 5.7 to 6.2 Gm., the plasma albumin from 2.9 to 3.4 Gm. per 100 cc.

Although the venous pressure had not decreased (192 mm. of saline on September 7 compared with 185 mm. on admission), digifolin was discontinued on September 10. Some respiratory distress persisted for another two weeks, but gradually subsided.

Because the tongue had remained sore and some ulcers on the margin were still present, 25 mg. of folic acid by mouth were given daily from September 26 to November 7. After the middle of October, the tongue no longer caused any discomfort.

By the end of October, edema and liver enlargement had completely disappeared. The heart was smaller, and the venous pressure was normal. The urinary albumin had decreased from 0.85 to 0.07 Gm. per 1000 cc.; the total plasma proteins had risen to 7.1 Gm. per 100 cc. The patient felt well and was able to take short walks without dyspnea or fatigue.

The weight, which had dropped to 62 Kg. (137 pounds) on October 2, remained constant for one month and then gradually rose. By November 21, it was 64.5 Kg. (142 pounds).

The amounts of chloride and sodium excreted in the urine had decreased very slowly (tables 2 and 3). In the eighth week after the rice diet was begun, the chloride concentration was 66.5 mg., the sodium concentration 32 mg. per 100 cc. of urine. The sodium-potassium ratio in the urine was 0.18. In the fifteenth week, the chloride concentration was 15.2 mg., the sodium concentration 1.3 mg. per 100 cc. of urine. The sodium-potassium ratio in the urine was 0.006.

The patient returned home on November 21. He was advised to continue the rice diet, to which one ounce of meat twice a week was added. Fluids were limited to 750 cc. per day.

Table 2

Urinary Chloride Concentration

Week of Rice Diet (Diet started Aug. 7, 1946)	*Mg. Chloride in 100 cc. of urine (averages)*
6th	81.7
7th	88.3
8th	66.5
9th	57.5
10th	35.2
11th	26.6
12th	18.7
13th	17.0
14th	18.8
15th	15.2
16th	15.7

Table 3

Concentrations of Sodium, Potassium, and Chloride in Blood, Serum, and Urine

	Eighth week of diet (Sept. 28, 1946)	*Fifteenth week of diet (Nov. 18, 1946)*
	milli-equivalents per liter	
Sodium:		
blood	84.3	81.7
serum	139.7	142.2
urine	13.9	0.57
Potassium:		
blood	46.2	50.0
serum	4.8	5.3
urine	45.0	57.2
Chloride:		
blood	84.0	79.3
serum	94.2	100.0
urine	14.0	4.1

Summary

The history of a patient with myocardial aneurysm following myocardial infarction is given. He was admitted to Duke Hospital in advanced cardiac failure with marked sodium chloride retention. For a period of seven months, four of which the patient spent in various hospitals, he had been treated with salt-"poor" diets, digitalis, ammonium chloride, theominal, aminophyllin, salyrgan, and a paracentesis. In spite of this treatment, the cardiac failure had become progressively worse and the patient had developed severe dyspnea, generalized anasarca, cardiac enlargement, liver enlargement, ascites, albuminuria, hypoproteinemia, hypocalcemia, and a decubitus ulcer. In five weeks of treatment with the rice diet, supplemented by vitamins and iron, the patient improved so much that digitalis, the only medication that had been continued, could be stopped. In nine more weeks, during which the patient was given no treatment except the rice diet, vitamins A, B, C, and D, folic acid, and iron, all signs and symptoms of cardiac failure disappeared.

A BASIS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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The diagnosis of rheumatoid arthritis means, too frequently, that the patient leaves the office of his physician with an attitude of uncertainty toward his future which, in this disease perhaps more than in any other, is prejudicial to his welfare. Vague and indefinite remarks as to possible causes and treatments can easily add to the worries of one whose burdens are already heavy. The physician should recall the maxim of Oliver Wendell Holmes: "Give your patient the benefit of your knowledge; keep your doubts to yourself." A confession of ignorance often offers a more substantial basis for therapy than that derived from an edifice of doubtful theories. The fact that our present knowledge of specific causative agents and mechanisms in arthritis is extremely limited does not mean that the physician can offer nothing to the patient. There are many classical examples—typhoid fever and tuberculosis might be cited—of diseases which were recognized from purely clinical findings by several generations of physicians before the chief etiologic agent was discovered.

A review of the various classifications of arthritis published during recent years[1] reveals that their bases are largely descriptive and that there are many unknown factors in those instances where the cause of the joint disease is classified as *known*. Bauer's[2] classification, which is the broadest and most practical, insists on "a detailed medical history and a complete physical examination" and warns against "the patient's diagnosis of rheumatism or arthritis." Then the clinician must decide whether previous injury to the joint is important enough to place the affection in the class of *known etiology (traumatic)* or whether it belongs in the class of *unknown etiology*, either as *secondary degenerative joint disease* or as *atypical rheumatoid (proliferative or chronic infectious) arthritis*. The emphasis on descriptive criteria is exemplified by the statement:

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1. Hench, P. S. et al.: The Present Status of the Problem of "Rheumatism": a Review of Recent American and English Literature on "Rheumatism" and Arthritis. Ann. Int. Med. 8:1315-1374 (April); 1495-1555 (May) 1935.
2. Bauer, Walter: The Diagnosis of the Various Arthritides. New England J. Med. 221:524-533 (Oct. 5) 1939.

"If one will allow for the passage of time before making an absolute diagnosis, the true nature of the type of arthritis present will become all too apparent." This statement refers to the differences between *atypical* and *typical* rheumatoid arthritis.

Such statements and classifications, the products of careful studies and analyses by groups of experienced clinicians, are discouraging if one expects to offer his patients a specific treatment for every complaint. To the physician who recalls that the practice of medicine is an art requiring his particular skill in assisting a patient to face the unknown, the problem of rheumatoid arthritis is a challenge. There is no real basis for pessimism, and it is clear that many advances in the treatment of arthritis have been made during the last decade, when students of the disease have emphasized their failures to accumulate proof for the theory of focal infection[3]. This theory, first propounded in 1912[4], is often foremost in the mind of the patient, but after some twenty-five years of enthusiastic testing it has not been substantiated as an adequate explanation of rheumatoid arthritis. Other scarcely less publicized theories and quasi-specific treatments such as colonic irrigation, vaccines, sulfur, and super-irradiated sterols also have failed to meet the tests of controlled studies.

The Advantages of Taking the Patient into One's Confidence

It now seems that the best approach to treatment is that in which the physician gives more thought to the advantages of taking the patient into his confidence, so that they together can face and work out the problems presented by a disease of unknown cause. The physician usually will find that he has made a friend. Arthritics lead a lonely life. They are—or occasionally fancy themselves to be—mainstays of their families, and of many community and business activities. Being perfectionists, they often have formed the habit of driving themselves, tending to compete with their own ideals rather than with their contemporaries. They are seldom overly sensitive about their joint deformities, and they seem to resent the handicap to their projected activities more than the pain and anatomic changes associated with their disease. They continuously fight disability and welcome an ally in the battle. They never willingly relinquish the management of their own condition and are quite sensitive to the attitude of a physician who initiates a transiently beneficial type of treatment in the hope that another physician will be consulted for the next exacerbation. Such features of the arthritic's personality often are so outstanding that the family physician, who recognizes both these attributes and the presence of rheumatoid arthritis, may find it wise to postpone a detailed discussion until the patient has accumulated enough experience to be receptive.

A second advantage to the physician of taking the patient into his confidence will be an altered attitude on the part of the patient. His feeling that the medical profession is withholding beneficial treatment, because some acquaintance has been "cured" by this or that removal or injection, will be removed. The patient's identification of himself or herself with the thousands of fellow-sufferers who are being helped to overcome other diseases for which no specific treatment is available is a step toward improvement. In this way the patient often can be induced to assume an attitude similar to that of a tuberculous patient who is being treated in the home. He may come to appreciate that, in compensation for his pain, his disease allows him some activity and does not carry the risk of infection to others.

The greatest advantage is that a state of uncertainty, incompatible with any type of contentment in life, can be changed to a much more satisfying philosophy if our available knowledge of the disease is presented properly to the patient. Much of the dissatisfaction of present-day sufferers from arthritis arises from the false hopes engendered by the enthusiastic attitude of a previous generation of the medical profession toward the theory of focal infection, and by their belief that "the cause can be found." Patients can be made to understand that such studies have increased our knowledge of the disease to a certain point, and that we must now consider the unknown factors in the patient himself.

3. Cecil, R. L. and Angevine, D. M.: Clinical and Experimental Observations on Focal Infection, with an Analysis of 200 Cases of Rheumatoid Arthritis, Ann. Int. Med. 12: 577-584 (Nov.) 1938.
4. Billings, Frank: Chronic Focal Infections and Their Etiologic Relations to Arthritis and Nephritis, Arch. Int. Med. 9:484-498 (April) 1912.

Therapy Based on the Factor of Resistance

Once the existence of an unknown factor in the causation of rheumatoid arthritis is accepted, it is apparent that there must be inherent in the human body an almost equally potent antagonistic factor. The rapid return to a normal or quiescent stage, frequently seen after the removal of some burden which the patient has been carrying, often parallels the responses seen after the institution of an equally non-specific rest therapy in pulmonary tuberculosis. The fact that a few patients with tuberculosis show only slight evidences of resistance to the infection and grow steadily worse should not discourage the institution of a positive plan of treatment, with assurance to the patient that beneficial results are expected. Similarly, those instances in which the rheumatoid arthritis progresses inexorably from joint to joint should not blind us to the strong recuperative tendencies evidenced in a large proportion of patients having the disease.

This simple concept that there is present in the human body some definite mechanism of resistance to arthritis, analogous to that responsible for the arrest of tuberculosis, is the outstanding feature which should be presented to a patient in instructing him about his disease. Such a concept can be derived rationally only if one starts with the premise that the arthritis is of unknown cause and that no form of treatment can be regarded as specific. On such a basis, a plan of therapy for both the patient and the physician is clarified.

Teaching the patient the art of living

For three or four centuries experienced physicians have emphasized the need, in prevention and in treatment of chronic diseases, for the patient to learn and the physician to teach the art of living. The sufferer from arthritis most often becomes an eager pupil, and his physician should make a real effort to qualify as a teacher. He can do so only if he is willing to familiarize himself with the personal history[5] as well as the medical history of his patient and to take almost infinite pains in evaluating the relative importance of emotional and situational burdens, in addition to those implied by the presence of active local infections, handicaps to locomotion and proper posture, and undesirable habits of diet, work, sleep, and the like. The importance of "a different point of view on the part of both physician and patient"[6] in the treatment of chronic disease has been emphasized repeatedly[7]. Too great emphasis cannot be placed on the fact that, in treating arthritis, it is the physician's responsibility, as it always has been, to assist his patient to face the unknown.

When it is clear that the aim of treatment is to assist, in every way possible, those unknown but natural factors of resistance which are able to produce quiescence or arrest in the arthritic process, the relative importance of different features of the treatment can be estimated. In some instances it may appear that infection in the tonsils should be given precedence; in others the need for more sleep or a better bowel routine may seem to be of the greatest importance. Some patients need rest; others would be harmed by what that word implies, but are more in need of repose in the sense of peace of mind. Many need, more than anything else, the relief of pain and assurance of improvement of their deformities and disabilities which modern orthopedic and physical medicine can offer. Every patient needs the continued interest of a physician who will encourage a mode of life which is planned to prevent any type of depletion.

Non-specific therapeutic measures

Under circumstances in which a maximum effort to improve all features of the patient's life is being made, there would seem to be a place for trial of some of the non-specific measures which have been credited with promoting remissions. Therapy with gold should not be offered until the patient is capable of understanding its place in the scheme of treatment, but a remission in association with chrysotherapy may simplify the many other adjustments which are necessary to encourage both patient and physician in further efforts aimed at the more difficult problems.

Summary

If careful and complete diagnostic studies fail to reveal an obvious and satisfying cause for an arthritic manifestation, it is often

5. Heath, C. W.: An Interview Method of Obtaining Personal Histories, New England J. Med. 234:251-257 (Feb. 21) 1946.

6. Ropes, M. W. and Bauer, W.: Rheumatoid Arthritis: Its Various Clinical Manifestations, New England J. Med. 233:592-596 (Nov. 15); 618-623 (Nov. 22) 1945.

7. (a) Minot, G. R.: General Aspects of the Treatment of Chronic Arthritis, New England J. Med. 208:1285-1290 (June 22) 1933.
(b) Pemberton, Ralph: Developments in Arthritis, Am. J. M. Sc. 209:364-382 (March) 1945.

best to regard the disease as one of unknown cause and to explain this concept to the patient in such a way that he will not persist in searching for a specific remedy. This explanation is important in teaching a patient to adjust to the local handicaps of degenerative joint disease (*osteoarthritis*). It is also essential as a basis for the always detailed and often extensive revision of environmental and psychological factors which is necessary to encourage remission and quiescence in rheumatoid arthritis.

THE TREATMENT OF PSYCHOGENIC HEADACHES

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Headache is one of the commonest complaints with which the average physician is confronted. Most of us, including myself, have experienced difficulty in dealing effectively with this complaint because of a tendency to focus attention upon some particular aspect of the problem and to neglect other aspects which may be of equal or greater importance. The factor most frequently neglected in the treatment of headache is the personality of the patient and the relationship of life situations to his headaches. From personal experience every layman knows that certain trying situations associated with tension, anxiety, or resentment may precipitate a headache. Yet, too often, the cautious physician overlooks this simple and common cause of headaches and subjects his patient to a battery of diagnostic procedures, thus unwittingly increasing the patient's anxiety and often aggravating his headache.

Headache Mechanisms

To evaluate the role which psychogenic factors may play in the production of headache, it is necessary to review the basic physiologic mechanisms which may cause this symptom in the absence of organic disease in or about the head.

Wolff and his coworkers[1] have shown that the headaches of migraine and hypertension are due primarily to distention and dilatation of branches of the external carotid artery, and that changes in the intensity of headaches are related directly to changes in the amplitude of pulsations in the temporal and occipital arteries. Factors which decrease the amplitude of pulsations, such as digital pressure on the superficial branches of the external carotid artery and the injection of vasoconstrictor drugs, particularly ergotamine tartrate, also decrease the intensity of the headache. Raising the intracranial pressure, which dampens the pulsations of the intracranial arteries and relieves experimental histamine headache, has no effect on the headaches of migraine and hypertension. Scotomata preceding headaches were shown to be due to cerebral vasoconstriction, since they were temporarily abolished by inhalation of small amounts of amyl nitrite.

The same investigators, using various experimental procedures, have produced sustained contraction of the muscles of the scalp and neck, evidenced by increased electromyographic activity, associated with pain in various parts of the head and neck. It was found that in patients suffering from sinusitis, migraine headache, and emotional tension, there is sustained contraction of the neck and scalp muscles, with concomitant pain in the neck and over the back of the head. In a study of the mechanisms of chronic post-traumatic headache, Simons and Wolff[2] found that, with the exception of those headaches associated with subdural hematoma and subarachnoid hemorrhage, the chronic headache following trauma to the head results from sustained contraction of the skeletal muscles of the head and neck associated with the occurrence of sustained resentment, anxiety, frustration, tension, and fear. In many cases the amount of muscle contraction is minimal and probably causes headache only because it is sustained and because of an abnormal preoccupation with the head.

Allergic sensitivity is generally considered to be a cause of chronic headache, and there have been enthusiastic reports of the prevention of migraine and other headaches by the methods employed in the treatment of allergic disorders. Unfortunately, little attention has been paid to the accurate classification of headaches claimed to be of allergic origin, or to the mechanism by which allergic sensitivity might cause headache. In

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1. Wolff, H. G.: Mechanisms of Headache, Arch. Neurol. & Psychiat. 50:224-232 (Aug.) 1943.

2. Simons, D. J., and Wolff, H. G.: Studies on Headache: Mechanisms of Chronic Post-Traumatic Headache, Psychosom. Med. 8:227-242 (Jul.-Aug.) 1946.

other allergic conditions, such as urticaria and bronchial asthma, histamine, or a histamine-like substance, is thought to be responsible for the tissue reactions. Histamine, when injected intravenously in normal individuals, is known to produce marked dilatation and increased pulsation of cranial arteries, accompanied by generalized headache. Wolff and his co-workers have demonstrated that this experimental histamine headache is due to stretching of pain-sensitive structures in the walls of the intracranial arteries. Headaches associated with fever have a similar mechanism.

In 1939 and 1941 Horton[3] reported observations on "a new syndrome of vascular headache," which he called "histaminic cephalgia," characterized by frequently occurring, hemicranial headaches of short duration, beginning in the latter decades of life, involving the eye, the temple, the neck and often the face, and tending to conform to the ramifications of the external carotid artery, the superficial branches of which are dilated and tender. Characteristic attacks were reproduced by the *subcutaneous* injection of 0.3 to 0.5 mg. of histamine, and these, as well as the spontaneous attacks, could be completely controlled by the intravenous injection of adrenalin and other vasoconstrictor drugs. Desensitization to histamine was reported to have brought complete relief to 48 of 63 patients for varying periods. On the other hand, there have been several observations indicating that the *intravenous* injection of 0.1 mg. of histamine tends to reproduce headaches due to various causes, suggesting that histamine acts as a headache-producing agent only by virtue of being a powerful vasodilator and not from a specific sensitivity reaction.

Psychogenic Factors in the Etiology of Headache

It is obvious that physiologic mechanisms known to be implicated in certain types of "functional headache" only explain *how* the patient has headache; they fail to explain *why*. To complete the picture, it is necessary to understand the psychodynamic factors which commonly activate one or more of these physiologic reactions.

The psychoanalytic studies of Fromm-Reichmann[4] indicate that *subconscious hostility* is a significant finding in patients with *migraine*. These individuals have a marked hostility, of which they are not consciously aware, for some person to whom they are closely attached. Often the migraine patient comes from a conventional family with strong solidarity and family pride, in which aggression against one another is forbidden. If one member dares to express hostility against another, he is punished by exclusion, and the fear of such punishment is enough to keep his hostilities repressed. Then, when anger is aroused and cannot express itself adequately, the individual takes it out upon himself, so to speak, in an attack of migraine. Later in life any situation calling for aggression is likely to provoke the same mechanism.

Wolff[5] reported that a psychobiologic study of 46 subjects with migraine revealed them to be peculiarly prone to development of pernicious emotional states, either sustained or episodic; in certain of them a sudden increase in stress was provoked by clearly definable life situations, and such periods were associated with an increase in the intensity and frequency of attacks. More than nine tenths of his subjects had "set" personalities, with perfectionism and a desire to have things "just so" as outstanding characteristics. Ross and McNaughton[6], using the Rorschach method, found that "items associated with migraine can be seen as representing persistence toward success, difficulty in sexual adjustment, perfectionism, inflexibility, conventionality, and intolerance."

The following case history serves to illustrate these principles:

A 26-year-old, married advertising and sales-promotion manager of a retail chain store complained of paroxysmal headaches associated with nausea and vomiting and preceded by visual disturbances and localized areas of numbness. Attacks began with "glimmering" of vision and inability to focus, lasting half an hour. During the next half hour he experienced numbness of one hand and of one side of the lips and tongue, either left or right, associated with slight thickness of speech. As the numbness disappeared a severe headache developed on the opposite side, localized in the fronto-temporal region and associated with nausea and vomiting. During

3. (a) Horton, B. T., MacLean, A. R., and Craig, W. M.: A New Syndrome of Vascular Headache: Results of Treatment with Histamine, Proc. Staff Meet., Mayo Clinic, 14: 257-260 (April) 1939; (b) Horton, B. T.: The Use of Histamine in the Treatment of Specific Types of Headaches, J.A.M.A. 116:377-383 (Feb. 1) 1941.

4. Fromm-Reichmann, F.: A Contribution to the Psychogenesis of Migraine, Psychoanalyt. Rev. 24:26-33 (Jan.) 1937.

5. Wolff, H. G.: Personality Features and Reactions of Subjects with Migraine, Arch. Neurol. & Psychiat. 37:895-921 (April) 1937.

6. Ross, W. D., and McNaughton, F. L.: Objective Personality Studies in Migraine by Means of the Rorschach Method, Psychosom. Med. 7:73-79 (March) 1945.

the attacks of headache, which usually lasted about one hour, he had noticed increased prominence of the temporal artery on the side of the pain.

He had had one such attack at the age of 15 or 16, two in July, 1946, and four between October, 1946, and January, 1947. In 1940 he developed symptoms of peptic ulcer, which was not diagnosed until 1942, when he was medically discharged from the army with a diagnosis of "duodenal ulcer." After his discharge the ulcer symptoms disappeared, but he continued to have occasional attacks of indigestion and vomiting, which occurred whenever he got into an argument.

Physical and neurologic examination was entirely negative.

The psychiatric history revealed that the patient was an only child, brought up largely by his mother. His father, a railroad man, was away from home most of the time; when at home, he was a strict disciplinarian. The patient did not recall having any hostile feelings against his father until he was 15 or 16 years old, at which time his father began to drink excessively. The patient had to control him, and was always able to do so by reasoning with him. His first attack of migraine occurred at about this time. Since then his father has died. In 1940, while the patient was attending art school, a classmate developed an acute psychosis, and after this the patient became very nervous and had transient phobias of losing his mind. He recalled that his gastrointestinal symptoms appeared at that time. His two migraine attacks in July, 1946, immediately followed the completion of a highly successful advertising campaign which placed his store second highest in the nation and resulted in his being recommended for transfer to a new branch store which was being opened. His transfer became effective in October, and since then he has had four attacks. He has had difficulty in getting along with his new store manager, and he related one of his attacks to a specific situation in which the boss had criticised his work.

The personality inventory revealed compulsive and perfectionistic traits. He said he could not tolerate being in a room that was untidy. When leaving home he would frequently go back to see if he had turned off the lights and locked the door. When he tackled a job he always worked incessantly until it was finished and was not satisfied until it was as near perfect as possible. He also stated that for some time—he could not remember how long—he had shunned arguments by walking away. Whenever he became involved in an argument he would vomit afterward.

This patient described classical migraine attacks. His first attack was related to feelings of resentment toward his father, and his recent attacks occurred in the presence of resentment toward his boss, or father surrogate. He is a compulsive perfectionist who represses his aggressive impulses by walking away. His attacks of vomiting following arguments possibly represent what has been called "abdominal migraine." In my experience migraine is frequently associated with other psychosomatic conditions, and it is of interest that this patient gave a history of duodenal ulcer.

In contrast to the paroxysmal, migraine-type headaches, *tension headaches,* arising from sustained contraction of the muscles of the scalp and neck, tend to be constant over long periods. They are commonly associated with *sustained emotions* of resentment, anxiety, frustration, and depression. Constant headache may also be a complaint of patients with conversion hysteria, neurasthenia, mental deficiency, or simple schizophrenia. In these conditions the headache is often described as having a hat-band distribution or being localized at the vertex, and as giving a sensation of pressure or boring. It is usually impossible to demonstrate any physiologic headache mechanism in these cases, or even to be certain that the sensation described is actual pain, and one is forced to the conclusion that the complaint is symbolic of the individual's inadequacy and inability to adjust to his environment.

Diagnosis

In the differential diagnosis of headaches the most important distinction is between headache symptomatic of organic disease and "functional" headache. The more common causes of organic headaches are various brain lesions, inflammation of the meninges and bones of the skull, sinusitis, and temporal arteritis. Except in cases of disease of the upper cervical vertebrae, pain is never referred to the head from organs outside of the head, although disease of remote organs associated with fever or absorption of toxic products may give rise to vascular headaches by causing dilatation of intracranial arteries.

In practically all cases of *organic* headache the history, physical examination, and laboratory studies reveal the correct diagnosis. X-rays of the skull are always indicated in doubtful cases, both to reveal or to rule out hidden lesions and to assure the anxious patient that nothing has been overlooked. Spinal puncture is occasionally indicated but should be used with discretion in patients suspected of having psychogenic headaches, since these patients frequently develop incapacitating post-puncture cephalgia.

Functional headaches must be differentiated into (1) those in which the immediate cause is a disturbed vascular mechanism, such as migraine, hypertensive vascular disease, "histaminic cephalgia," and possibly allergy; (2) those in which the headache is due to sustained contraction of the muscles of the scalp and neck associated with emo-

tional tension; and (3) those in which the headache is symbolic of some subconscious emotional complex. Vascular headaches are always paroxysmal, whereas purely psychogenic headaches may be either intermittent or constant. Patients with psychogenic headaches usually have other symptoms which are quite obviously psychogenic, and neurologic examination may reveal certain findings characteristic of hysteria.

The Psychotherapy of Headaches

I confess to being an amateur in the art of psychotherapy, my experience being limited almost entirely to the management of headache problems. As a clinical neurologist, both in civilian practice and in the army, I have found that a large part of my work is concerned with headaches, and I have gradually developed the conviction that the vast majority of these must be dealt with on a psychobiologic level. Adolf Meyer, in his teaching of psychobiology, emphasized the principle of "levels of integration," which he classified as "the anatomical, the physiological and the psychobiological." In his discussions of therapy he stressed the importance of treating the patient on the level of integration which is primarily disturbed. Headache is a symptom, not a disease; as such, it stands on a physiologic level and can sometimes be effectively treated on this level by altering the headache mechanism through the use of vasoconstrictor agents, by overcoming the individual's sensitivity to histamine, or by the treatment of a specific allergic sensitivity. This statement has been amply proven by clinical experience. However, one sees numerous cases of headache in which attempts to alter a known headache mechanism are ineffective or in which no physiologic disturbance can be demonstrated. Such cases require investigation and treatment on a psychobiologic level, and when this investigation is undertaken it is soon discovered that the symptom of headache is merely a superficial expression of maladjustment or emotional illness.

The first step in the psychotherapy of headaches is to obtain a detailed life history of the patient from a social and psychiatric point of view, complemented if possible by statements from relatives. An attempt is made to correlate the onset and exacerbations of all psychosomatic symptoms, including headache, with environmental situations conducive to stress, tension, anxiety, disappointment, frustration, or hostility. Explanation to the patient of the psychogenic origin of his headaches is best deferred until all the material is available, since many patients resist and resent a pychogenic explanation and it is necessary to prove to them that the diagnosis is correct. In some cases, where the headaches are of relatively recent onset and the personality structure is essentially sound, the mere demonstration to the patient of the causal relationship between environmental stresses and the occurrence of headaches, and the patient's acceptance of this relationship, is sufficient to stop the cycle, and no further therapy is necessary. On the other hand, patients with headaches of many years' duration, particularly patients with low intelligence, continue to resist and argue after all the evidence has been presented. It is my experience that further psychotherapy is a waste of time in such cases and that actually the patient does not want to be helped.

If further psychotherapy appears to be indicated, and if practical considerations permit, the next step is to work out in a series of interviews, preferably at weekly intervals, the patient's basic psychologic difficulties. In civilian practice it is usually impossible to change the environmental situation, so the patient must be taught how to make a better adjustment to existing conditions. In patients who are severely repressed and do not give out information easily, I have found that one or more interviews under intravenous sodium amytal, given slowly until the inhibitions are removed, frequently reveal basic emotional conflicts which the patient had previously concealed. This technique is particularly valuable at times when the patient is suffering from a headache and when the repressed emotional conflict is acute. The mere discussion of this material, with release of the associated emotion, often relieves the patient of a large amount of anxiety, establishes closer rapport with the physician, and permits freer discussion in subsequent interviews. In the course of psychotherapy the presenting symptom is often alleviated without any particular attention's being paid to it, but manifestations of anxiety, which may have been minimal or absent, may become aggravated and distressing. It is well to forewarn the patient of this possibility and to assure him that his anxiety will diminish as treatment progresses.

The results of psychotherapy in cases of headache do not lend themselves to statistical analysis. Success depends upon many variable factors, including the patient's personality structure, his degree of insight, the alterability of his environment, and the amount of time and interest which the physician can devote to his problems. All these factors must be taken into consideration before treatment is undertaken. With a little experience, one can select for brief psychotherapy those patients who appear likely to be benefited—such as those with simple tension and anxiety states—and refer for more thorough psychologic analysis those whose personality disorder appears to require it.

THE RECOGNITION AND MANAGEMENT OF SUBARACHNOID HEMORRHAGE

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Subarachnoid hemorrhage develops usually as a grave medical emergency whose management is conditioned by time and the possibility of determining the cause and location of bleeding. Prompt decisions are therefore necessary regarding measures to relieve pain, insure rest, and maintain vital functions while the advisability of more specific diagnostic and therapeutic procedures can be determined. Hospitalization is essential to these ends, even though some risk of aggravating hemorrhage may be incurred *en route*.

Etiology

Blood may escape into the subarachnoid space directly from cerebral vessels or by extension from intraventricular or intracerebral hemorrhage. "Spontaneous" hemorrhage consequently may follow rupture of a vascular defect, such as a congenital aneurysm or angioma; or it may result from degenerative, septic or neoplastic erosion of the blood vessel wall, increased vascular permeability (toxic or nutritional), or purpuric blood dyscrasia. Congenital aneurysm predominates as a cause in the younger age group; hypertensive or arteriosclerotic vascular disease, in the older. Traumatic subarachnoid bleeding is fundamentally a neurosurgical problem which deserves separate consideration.

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Pathologic Physiology

The clinical manifestations, both irritative and mechanical, of subarachnoid hemorrhage are determined by the site, degree, and duration of bleeding, as well as by its etiology. Intracranial and intraspinal pain-sensitive structures are stimulated to produce headache, radicular pain, and meningismus. Cortical irritation is responsible for apprehensive restlessness, disturbances of the sensorium, muscular twitching, and sometimes convulsions. Local accumulation of blood may compress or displace intracranial structures to produce a variety of neurologic signs.

Continued subarachnoid bleeding is incompatible with survival; in fact, some observers[1] feel that the duration of arterial leakage must be exceedingly brief to permit recovery, because surviving patients seldom show increased intracranial pressure. Blood is removed from the subarachnoid space normally by the comparatively slow process of phagocytosis. With excessive bleeding, therefore, clots accumulate in the basal cisterns, debris clogs the pacchionian filters, drainage and absorption of spinal fluid are impeded, and increased intracranial pressure follows to produce intracerebral venous stasis and even hemorrhage. In addition, reactionary edema may develop in the cerebral tissues underlying the clot, to increase intracranial congestion. When brain swelling is marked, the hippocampal gyri will herniate between the tentorium and the midbrain, compressing vital diencephalic and brainstem structures. Venous outflow from the posterior fossa is then further embarrassed, and intramedullary venous hemorrhages may occur.

Symptoms and Signs

Premonitory symptoms may precede subarachnoid hemorrhage, but few are specific. Recurrent headaches of the migraine type, associated with transitory diplopia (sometimes called "ophthalmoplegic migraine"), are invariably caused by distention of an intracranial aneurysm. In these cases, arteriography and surgical treatment may be possible before rupture takes place. Unfortunately, however, most patients are seen only after leakage has occurred.

Presenting symptoms, occasionally attributable to physical or emotional stress, de-

1. Kemp, R.: The Lumbar Puncture Pressures in Subarachnoid Haemorrhage, Lancet 2:1369-1371 (Dec. 11) 1937.

velop abruptly with violent throbbing or "bursting" headache accompanied by dizziness, nausea, and vomiting. Pain may be referred to the neck, back, or even to the extremities. Photophobia and fearful restlessness may be followed in minutes or hours by confusion, delirium, stupor, and coma. In some instances, symptoms may abate after a day or two, only to recur with a second hemorrhage — often the result of uncontrolled restlessness. A more insidious onset may simulate that of septic meningitis, especially when fever and meningismus appear.

Examination is often limited by the patient's critical condition. Predisposing disease, such as hypertension, arteriosclerosis, cutaneous telangiectasia, or purpura, may be evident. Sweating and prostration are common. Passive anteflexion of the head meets resistance, and a mild Kernig sign may be found. Fever appears—first as a foreign body reaction, later as a result of dehydration, central disturbance of thermal regulation, or aspiration pneumonia. Relative bradycardia, due to increased intracranial pressure, may give way to tachycardia associated with hyperthermia in the end. Respiration, which is rapid at first, may later become periodic and finally gasping. Blood pressure fluctuates with intracranial dynamics, rises with increasing intracranial pressure, and falls as a terminal event.

From a neurologic standpoint, significant findings are few. Congestive changes appear in the fundi; sometimes papilledema is seen. Characteristic retinal or subhyaloid hemorrhages may follow rupture of the central retinal vein, often on the side of intracranial bleeding. Cranial nerve palsies, when present, may also help to determine the side of hemorrhage. Pupils may be unequal, the larger being on the affected side. Miotic pupils indicate ventricular or pontine hemorrhage. Dysphagia, with suppression of gag and cough reflexes, is conducive to aspiration of throat accumulations. Motor function is often suppressed; tremors or twitching are frequent, although convulsions are rare. Flaccid paralysis of one side and deviation of the head and eyes toward the lesion give evidence of associated intracerebral bleeding. (Intrapontine hemorrhage is distinguished by crossed hemiplegia, with head and eyes deviated away from the lesion.) Decerebrate rigidity and release of postural neck reflexes may accompany the development of a tentorial pressure cone. Tendon reflexes initially are sluggish or absent as a result of cerebral shock. Later, their activity may fluctuate along with the development of pyramidal tract signs—extensor plantar responses and absent superficial abdominal reflexes. These signs seldom render localizing value.

Differential Diagnosis

Conditions to be considered in the differential diagnosis might include aseptic meningitis, encephalitis, and even hysteria, all of which can be eliminated by diagnostic lumbar puncture. Rarely, spinal fluid may contain a few red cells in "hemorrhagic encephalitis" following any one of a number of severe infections, such as influenza and scarlet fever. Various causes for coma should be considered in the unconscious patient, including head injury, epilepsy, diabetes, and uremia. A history of progressive personality change prior to ictus may suggest a frontal lobe tumor, particularly glioblastoma multiforme. Bleeding into such a tumor may occur, and sometimes reaches the subarachnoid space.

Laboratory Findings

Spinal fluid examination is essential for diagnosis and treatment. The findings depend upon the severity and duration of hemorrhage[2]. Initial pressure may vary from normal to 700 or 800 mm., averaging about 300 mm. of water. Blockage of the subarachnoid space by clots may cause slow drainage and a poor Queckenstedt response. The "bloody tap" is distinguished by clearing of the turbidity of the draining fluid and by a lack of supernatant xanthochromia. Uniformly or increasingly bloody fluid characterizes true subarachnoid bleeding, and supernatant fluid becomes xanthochromic three to four hours after ictus. The number of red cells in the spinal fluid should be determined for comparison with findings at subsequent spinal punctures, in order to ascertain cessation or recurrence of hemorrhage. The ratio of white to red cells in the fluid first parallels that in the circulatory blood; later (seven to ten days), the foreign-body pleocytosis may simulate that of septic meningitis.

2. Merritt, H. H. and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Co., 1937.

Laboratory studies otherwise may contribute little, although hemoconcentration may indicate dehydration. In some instances, tests for capillary fragility and for the bleeding and clotting time may be desirable. Investigation of the nonprotein nitrogen content and the carbon dioxide combining power of the blood is indicated if renal damage is suspected. X-rays of the skull infrequently demonstrate calcification of earlier thrombosed aneurysmal defects. In patients suspected of having an aneurysm, arteriography should be deferred four to six weeks after bleeding has stopped.

Prognosis

Unfavorable prognostic signs include: (1) coma lasting over forty-eight hours; (2) steadily rising temperature, increasing pulse rate, periodic or irregular respiration, and falling blood pressure; (3) initially high spinal fluid pressure; (4) evidence of severe neurologic damage (hemiplegia, decerebrate posture); (5) aspiration pneumonia or atelectasis, and (6) detrimental coexisting disease, such as hypertension, polycythemia vera, or septicemia. In the absence of these signs, the outlook for recovery may be better —especially if specific measures to control bleeding are possible. Leaking aneurysms offer the least pessimistic outlook, with a mortality rate approaching 50 per cent[3].

Treatment

Treatment should be given forthwith, regardless of prognosis. Pain and shock require immediate attention and are best controlled by morphine[4], which is contraindicated only in coma. Chloral hydrate or barbiturates may be tried in cooperative patients. Hyoscine or atropine counteracts nausea and vomiting, and retards bronchial secretions. Control of anxiety and restlessness, which promote bleeding, should be established by either intravenous sodium amytal or paraldehyde, and maintained by paraldehyde given rectally as often as needed. Mechanical restraint is to be avoided. Vomiting is a constant hazard, and it is advisable to give nothing by mouth for the first few days; thereafter, small liquid feedings may be started. Since most patients with dysphagia expire, tube feeding is seldom warranted. Marked dehydration and acidosis should be avoided, but limitation of fluids to 1500 cc. daily is recommended. This amount should be given in the form of intravenous saline with 10 per cent glucose, one ampule of Solu-B, and 500 mg. of ascorbic acid. The efficacy of specific measures to promote clotting is questionable unless a purpuric condition exists.

The use of methods for relieving increased intracranial pressure and cerebral congestion is controversial. Some insist that lowering of the spinal fluid pressure by lumbar puncture may promote hemorrhage[5]. Others use this procedure only for diagnosis and relief of headache[4]. Merritt[6] states that "there is no adequate physiologic basis for the hypothesis that removal of fluid by lumbar puncture tends to increase hemorrhage." He recommends repeated drainage until the spinal fluid pressure approaches normal. Actually, clinical improvement, especially with regard to headache, disturbance of the sensorium, and medullary embarrassment, often follows removal of spinal fluid. Our policy is to reserve therapeutic lumbar puncture until signs of increasing intracranial pressure appear. Spinal fluid drainage then may be performed if necessary several times daily, sufficient fluid being removed on each occasion to reduce the pressure by one half. Intravenous sucrose (50 per cent), given simultaneously, also helps to relieve cerebral edema. Stimulants such as caffeine sodium benzoate or coramine may be given as often as needed, though the patient is usually moribund when these are required.

Constant nursing care is imperative. A darkened room relieves photophobia, and cold applications to the forehead are comforting. Mouth care, clearing of the airway by suction, and care of the bladder and bowels are essential. The patient should be lifted onto the bedpan, and straining avoided by oil enemas if necessary. Elevating the head of the bed 12 inches may help to relieve cerebral venous congestion. Turning the patient carefully every hour and hyperventilating the lungs with the standard carbon dioxide-oxygen mixture aids pulmonary

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   (b) Richardson, J. C. and Hyland, H. H.: Intracranial Aneurysms. A Clinical and Pathological Study of Subarachnoid and Intracerebral Haemorrhage Caused by Berry Aneurysms, Medicine 20:1-83 (Feb.) 1941.
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5. Sands, I. J.: Diagnosis and Management of Subarachnoid Hemorrhage, Arch. Neurol. and Psychiat. 46:973-1005 (Dec.) 1941.
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ventilation. Respiration may be supplemented by nasal oxygen (5 liters per minute) if cyanosis develops.

Control of hemorrhage by manual carotid compression and later by careful carotid ligation should be considered if clinical signs or electroencephalography[7] indicate which side is the site of hemorrhage. The risk of massive cerebral infarction incident to such a procedure varies inversely with the patient's capacity to establish collateral circulation, and increases with age and vascular disease. When intracerebral hemorrhage or tumor is suspected, cerebral decompression with aspiration or resection may be lifesaving. Competent neurosurgical help, therefore, is always to be sought in such instances.

In convalescence, prolonged bed rest (four to six weeks) should be enforced. Too often a patient will disobey orders, resume activity prematurely, and promptly suffer a second and more severe hemorrhage. A quiet existence, aided by sedatives and the avoidance of all stress, should be encouraged for six to twelve months, or until an aneurysm or other vascular defect can be demonstrated by arteriography and treated surgically.

7. Woodhall, B. and Lowenbach, H.: Congenital Cerebral Aneurysms Lateralized by Electroencephalography. South. M. J. 36:580-587 (Aug.) 1943.

THE TREATMENT OF THE CHRONIC CONVULSIVE DISORDERS

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The treatment of epilepsy has, during the past decade, received new impetus from the discovery of additional anticonvulsive drugs. Detailed electroencephalographic studies have contributed new information about the cause of convulsions and have been of diagnostic assistance. However, the real pathogenesis of a convulsion is still obscure, and no specific cellular pathema has been demonstrated.

Differential Diagnosis of Convulsions

A convulsion is a manifestation of a disease, not a disease itself. It is due to abnormal discharges from neuronal cells in the central nervous system. Every individual is a potential epileptic because each has a convulsive threshold, which may be high or low. The borderline between the "normal" and the "epileptic" is, at times, quite indistinct. Most persons have had spontaneous muscular jerks and twitchings. These are larval seizures and occur most commonly with fatigue. The concept that every person has his own convulsive threshold is important in the management of the chronic epilepsies. However, it is also well known that fits of one kind or another may be an early manifestation of serious brain disease.

When an individual has a convulsion for the first time, the principal duty of the physician is to try to determine whether or not there exists an organic disease of the nervous system. A neurologic examination is essential, and various laboratory studies may have to be done. Should there be findings indicative of a localized brain disorder or signs of increased intracranial pressure, pneumoventriculography will be necessary to rule out an expanding intracranial lesion. Patients who have been subject to convulsions for years and are still normal, physically and mentally, do not present such a diagnostic problem. It should be stated that neither convulsions in themselves nor the usual drugs used for their control will produce mental deterioration. When such deterioration occurs, we are dealing with an organic disease of the brain, the seizures being only a manifestation of that morbid process.

For the adequate treatment of cryptogenic (idiopathic) epilepsy it is essential for the physician to obtain certain specific information from the patient or his family. This ought to include the following facts: (1) the type or types of seizures; (2) the frequency of the attacks; (3) the time of day, month or year when they occur most often; (4) the presence or absence of any form of epilepsy in the family history; (5) any extraneous factors known to precipitate the attacks; and (6) past and present medication and the results obtained from it.

Since seizures are caused by abnormal neuronal discharges and since there exist numerous groups of neurones, all with great specificity of function, it is clear why there are many types of epilepsy and epileptic "variants." The majority of seizures will fall within three main groups: (1) grand mal, (2) petit mal, and (3) psychomotor attacks. The grand mal attack is characterized by a generalized tonic-clonic convulsion with complete loss of consciousness. Petit mal usually

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consists of a transient loss of awareness, or a "blank spell," but there are other forms of these momentary minor seizures. In psychomotor epilepsy there exists, temporarily, an abnormal mental state accompanied by unusual motor manifestations.

Drug Therapy

It is impossible to control convulsions by prescribing just any kind of anticonvulsive medication to be taken indiscriminately. One must select the drug which is most effective against the type of seizure being treated. It ought to be given in the smallest amount that will adequately control the seizures, and at the time when the greatest benefit will be derived from it. If a patient is subject to more than one type of attack it may be necessary to prescribe, in proper ratio, two or more of the preparations at our disposal. A medicine that is highly efficacious for one patient may be almost useless for another. For this reason it is frequently necessary to try different drugs and various combinations until the most effective formula is found.

Grand mal

The best therapeutic agent for major convulsions is dilantin[1]. The usual adult dose is a 0.1-Gm. (1½-grain) capsule taken three times a day after meals. In severe cases a total of 0.5 Gm. in twenty-four hours may be required. The toxic effects of dilantin include giddiness, ataxia, skin rash and hypertrophy of the gums.

The barbiturate preparations have the most universal anticonvulsive action. Phenobarbital may be given in doses of 0.03 Gm. (½ grain) to 0.1 Gm. (1½ grains) three times a day. Mebaral[2] has been, in my experience, equally as good as phenobarbital, and it causes less drowsiness. The symptoms of toxicity are those common to the barbiturates. The usual dosage is 0.1 Gm. (1½ grains) two to four times a day. Should large amounts of the barbiturates be required, the resulting drowsiness can be offset by small doses of amphetamine sulfate (benzedrine). Under no circumstances should the barbiturates be discontinued abruptly, because this may precipitate a series of attacks.

The bromides are occasionally beneficial when other less toxic drugs have failed. The dose usually required ranges from 1.2 Gm. (20 grains) to 1.8 Gm. (30 grains) per day. The blood bromide level ought to be kept at about 40 mg. per 100 cc. The bromides are tolerated unusually well by epileptic patients, but symptoms of poisoning, such as headaches, mental confusion and a vesicular skin eruption, will be encountered if the blood bromide level becomes too high.

Petit mal

These minor seizures usually respond well to either mebaral or phenobarbital given in the proper dosage. Dilantin is useless against petit mal attacks, and may cause them to occur with greater frequency. A new drug, tridione[3], is efficient in controlling some cases of minor fits. The average dose is 0.3 Gm. (5 grains) three times a day. Toxic effects, which are infrequent, include gastric disturbances, skin rash, lassitude, and slight drowsiness. It has been reported to have caused fatal aplastic anemia and agranulocytosis; this serious complication is evidently rare, but patients who are taking this drug regularly ought to have periodic blood counts. In this clinic we have seen eosinophilia (5 to 20 per cent) associated with tridione therapy. A common side effect in adults, apparently harmless, is photophobia. This often makes it necessary for the patient to wear dark glasses when in bright light.

It is common for patients to be subject to both grand and petit mal attacks. In mild cases the barbiturates alone will often give adequate control of both. In the more severe cases it is necessary to use dilantin and one of the barbiturates, or dilantin plus tridione. Dilantin ought not to be used alone in patients who have both petit mal and grand mal seizures.

Psychomotor attacks

Psychomotor attacks seemingly are helped by all three drugs—dilantin, the barbiturates, and tridione—but often do not respond too well to any of them. Each of these three anticonvulsive substances ought to be tried alone, and in the various possible combinations. This trial-and-error method is often

1. Dilantin (diphenylhydantoin sodium—Parke-Davis) is marketed in 0.06-Gm. (½-grain) and 0.1-Gm. (1½-grain) capsules.

2. Mebaral (N-methylethylphenyl barbituric acid —Winthrop) can be obtained in pills containing 0.06 Gm., 0.1 Gm., and 0.2 Gm. (3 grains).

3. Tridione (3,5,5,-trimethyloxazolidine-2,4-dione —Abbott) is available in 0.3-Gm. (5-grain) capsules.

necessary before a formula can be found that is beneficial.

Management of Precipitating Factors

The recent enthusiasm over drug therapy ought not to eclipse other important points in the medical management of epileptic patients. Very often a carefully obtained history will reveal definite situations which, time and again, precipitate attacks. A few factors commonly incriminated are fatigue, loss of sleep, constipation, imbibition of alcohol, hunger, anxiety, and nervous tension. If any of these factors are found, and the patient can be persuaded to avoid them, then the drug requirement frequently will be lessened. Should such situations be unavoidable, an extra amount of anticonvulsive medicine should be taken by the patient when he knows that he is going to be vulnerable to epileptic seizures. In the female, attacks often are associated with menstruation. It is generally conceded, however, that the production of an artificial menopause is of no value in reducing the total number of attacks. The rational therapy is to increase the dosage of the medication when the seizures are anticipated. Some women need take dilantin for only about ten days in each month.

Conclusion

In this brief article it has only been possible to outline the general principles of treatment of the convulsive disorders. Every patient with epilepsy presents to the physician a problem which must be handled as a separate and individual one. It is important to impress upon patients who have convulsions that they are not afflicted with an unusual disease or with a condition that implies a psychopathic taint or a social stigma.

The treatment of psychoneurosis begins with the history and physical examination. Even if the physician is positive of the diagnosis, a careful history and physical examination will be found time-saving and of specific value during subsequent visits. The physician should be meticulous, patient, and personal in taking the history. In addition to the usual medical history, a careful account of the patient's life must be recorded. It may not be tactful during the first visit to begin at infancy and progress through the years, but within two or three visits the physician should know the patient almost as well as he knows a member of his own family. The physician who is willing to listen has no difficulty in getting the psychoneurotic to talk.—John D. Campbell: Everyday Psychiatry, Philadelphia, Lippincott, 1945, p. 142.

MODERN CONCEPTS OF THE TREATMENT OF PEPTIC ULCER

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For many years the medical profession has sought an answer to the problem of peptic ulcer. The pendulum has swung back and forth between medical and surgical treatment, as neither has proven entirely satisfactory. In the past there has been no general agreement as to how ulcers should be managed. There was a time when the treatment that a patient received was largely a matter of chance. If he happened to be admitted to a surgical service, operation was often advised, regardless of the nature or duration of the ulcer symptoms; if he were admitted to a medical ward, conservative treatment was generally employed until it became apparent that he would not recover under a medical routine. Some time ago gastroenterostomy was performed frequently, but because the results were unsatisfactory, this operation has been largely discarded except in elderly patients having pyloric obstruction of long standing. Within the past decade gastric resection has been the operation of choice in patients having intractable ulcer, but this procedure carries a definite mortality and recurrences are not uncommon. Recently vagotomy has been offered to the profession as a possible solution of the problem. It would seem desirable, therefore, to review briefly the whole subject of the treatment of ulcer in an effort to evaluate the various forms of therapy which are being employed today.

Until the etiology of a disease is fully understood, progress in the treatment of that disease is apt to be slow and discouraging. This statement is particularly true of ulcer. Although many contributing factors are recognized, the exact cause of the disease is still unknown. While many different and totally unrelated methods of treatment have been advised, the general principles laid down many years ago form the basis of medical treatment today. Briefly, there are: (1) rest, both physical and mental; (2) frequent feedings to prevent overactive peristalsis; and (3) neutralization of the acid gastric juices. To decide when medical measures

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should be employed and when surgery is indicated is frequently a difficult matter. Since the decision rests upon the merits of the individual case, the treatment of different types and complications of peptic ulcer will be discussed under separate headings.

Simple Duodenal Ulcer

Certainly the treatment of simple, uncomplicated duodenal ulcer is strictly medical. This statement is especially true in the young individual whose ulcer has been present for only a short period of time. Whenever possible, hospitalization should be urged to insure both physical and mental rest. The Sippy diet, or a modification thereof, is generally employed. Drugs are not particularly important, although the use of antispasmodics, sedatives, and amphojel or a similar preparation is customary. Tobacco should be forbidden, or at least restricted. If hospitalization is impracticable, similar treatment at home should be advised, though it should be recognized that the results of treatment in the home are sometimes discouraging. In some cases ambulatory treatment of a simple ulcer may be justified, but the patient should be warned that this is the least desirable method of all.

Healing of an uncomplicated ulcer is usually not difficult to accomplish. The problem is to prevent recurrences. Some patients who have a clear insight into the situation can, by careful attention to their diet and regulation of their lives, prevent a return of the ulcer. There is, however, a fairly large group of patients who, though they understand their problem, find it impossible to remain well when they return to their usual activities. The same factors, whether social, domestic, or economic, which operated originally to produce the ulcer are still present, and no amount of explanation by the physician or cooperation on the part of the patient will suffice to prevent a recurrence.

Chronic or Recurrent Duodenal Ulcer

The decision between medical and surgical treatment is always a difficult one in this group of cases. As was pointed out above, the usual recurrence will subside promptly under adequate hospital care. Certainly one should hesitate to subject a patient to operation if his illness can be handled properly by a few weeks of hospitalization. However, there are two types of patients who do not fall into this category. One is the patient whose ulcer does not respond to medical care and whose pain persists in spite of the best that the physician and hospital afford; the other is the patient whose ulcer symptoms subside under treatment, but promptly recur as soon as he resumes his usual activities. Both these groups of patients are candidates for surgery. The situation should be explained carefully and final decision left to the patient himself.

Once operation is decided upon, the type of surgery to be employed is the next problem. For the most part gastroenterostomy has been abandoned in this type of patient. Gastric resection has wide popularity, and is practiced throughout the country. Within the past two or three years, however, resection of the vagus nerves, by either the transthoracic or the subdiaphragmatic approach, has been advocated as a possible substitute for resection. Although the results of this operation have been dramatic to date, it must be emphasized that it is still in the experimental stage and cannot be evaluated properly until careful follow-up studies of at least five years have been conducted.

Ulcer with Hemorrhage

Certainly the usual patient with an upper intestinal hemorrhage is a medical problem. Bed rest, hospitalization, if possible, sedatives (not morphine) in the apprehensive patient, and a modification of the Meulengracht diet are usually recommended. While feeding should be started early, it is useless to give anything by mouth to the patient who is actively nauseated or actually vomiting blood. Should the hemorrhage be so profuse or prolonged as to cause shock, the general principles of the treatment of shock are employed.

In the young patient hemorrhage, while alarming, is rarely fatal. In the older individual with sclerosed vessels recurrence or continuation of the bleeding is much more frequent. While some writers advocate immediate surgery in patients of the older age group, our practice at Duke Hospital is to treat them conservatively until it becomes apparent that the bleeding will not cease. When we are satisfied of this fact, the patient is prepared for surgery by multiple transfusions, and a subtotal gastric resection is performed. It might be said with some

degree of truth that, given an adequate amount of blood and a good surgeon, no one should die of a bleeding ulcer.

The role of vagotomy in the treatment of recurrent hemorrhage is a matter of considerable interest. If, as seems to be true, resection of the vagus nerves will prevent recurrent hemorrhage in patients with chronic ulcer, the operation should certainly be seriously considered for a patient who has had multiple massive hemorrhages.

Obstruction

When pyloric obstruction results from a duodenal ulcer, the physician must decide whether the obstruction is due to swelling and edema or to scarring. Too often an x-ray study showing complete retention at six hours is interpreted as meaning that scar tissue is present. In young people and in patients with an ulcer of short duration, such obstruction is often due to an acute inflammatory process with edema and spasm. This type of obstruction will frequently respond promptly to adequate medical treatment, including continuous suction—or, if this is impracticable, nightly aspiration—in conjunction with a modified Sippy diet, antispasmodics, and amphojel. Certainly if pyloric obstruction is not due to actual scar tissue, operation should be avoided.

On the other hand, obstruction from scarring is an irreversible process and there is but one answer—surgery. In the older person a simple gastroenterostomy is the operation of choice, and the results are usually excellent. In a younger patient with high gastric acidity it is probably wiser to do a resection.

Perforation

The treatment of perforation is immediate surgery, although recovery has been reported in patients treated without surgery by keeping the stomach completely empty for several days with continuous suction. The usual procedure is simple closure of the perforation. To allow such a patient to return to an unrestricted diet and his usual routine is merely courting trouble. It is always wise to advise the patient to follow a modified Sippy diet and routine for many months following a perforation.

Gastric Ulcer

The patient with a gastric ulcer is always a difficult problem. A large ulcer on the greater curvature should be considered malignant, and a gastric resection performed. A small ulcer on the lesser curvature in a young person is probably benign, but if the ulcer fails to heal promptly the stomach should be resected. Because of the danger of malignancy, vagotomy probably should not be performed in patients with gastric ulcer.

Marginal Ulcer

One of the most serious complications of gastric surgery is the development of a marginal ulcer. The surgeon usually claims that the marginal ulcer is a medical problem, while the internist is equally insistent that it is the surgeon's responsibility. Such ulcers are difficult to treat medically; they frequently bleed or perforate, and the formation of a gastroenterocolic fistula is not uncommon. The usual medical measures are apt to have discouraging results. Conventional surgery entails taking down the enterostomy, resecting the ulcer, and performing another anastomosis. This is a difficult procedure and one which the surgeon does not particularly relish.

It is in patients with marginal ulcer that vagotomy has had its most brilliant success. These patients have usually had their ulcer for years, and have had numerous operations. The complete relief of pain which usually follows vagotomy is a blessing indeed. If the immediate, dramatic results which are routinely observed in this type of patient after vagus resection are maintained over a period of years, it goes without saying that this is the operation of choice in patients with marginal ulcer.

Summary

It has been said that surgery is but an episode in the medical treatment of peptic ulcer. Certainly this statement is true of the conventional surgical procedures usually employed today. The simple, uncomplicated ulcer is always a medical problem. In the absence of obstruction or perforation, surgery is never resorted to unless the patient has intractable pain which fails to respond to medical treatment, or unless he is one of those individuals whose social, domestic, or economic status is such as to render rehabilitation impossible by medical measures. It should be clearly understood that resection of the vagus nerves is still in the experimental stage; although the early results have

been dramatic, a number of years must necessarily elapse before the procedure can be accurately appraised.

Certainly we as physicians should realize that there is no rule of thumb to be followed, no dogmatic criteria to be laid down which can be employed blindly in the treatment of ulcer. Every case is a law unto itself, and the treatment of each patient must necessarily be decided upon the individual merits of his case.

THE TREATMENT OF ANEMIA

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Fundamentally, there are only three causes of anemia: (1) blood loss, (2) excessive blood destruction, and (3) insufficient blood formation[1]. The alterations in the red cell volume (mean corpuscular volume), cell shape, and hemoglobin content (mean corpuscular hemoglobin content, color index) are most important and are characteristic of the different types of anemia[2]. It is essential that the specific type of anemia be recognized before treatment is attempted.

For therapeutic purposes the anemias can be divided into three main groups: (1) the anemias which respond to iron or liver fractions insoluble in 70 per cent alcohol, (2) the anemias which respond to a liver fraction soluble in 70 per cent alcohol and to folic acid, and (3) anemias which do not respond specifically to iron, liver, or folic acid.

Anemias Which Respond to Iron and Crude Liver Extract

1. **Anemia of acute blood loss**
2. **Anemia of chronic blood loss**
3. **Nutritional anemias**
4. **Idiopathic hypochromic anemia**
5. **Anemia of vitamin deficiency**
6. **Anemia of pellagra**
7. **Anemia of thyroid insufficiency**
8. **Hypochromic anemia of pregnancy**
9. **Nutritional anemia of infancy**
10. **Hookworm disease**

The blood picture in this group of anemias is normochromic or hypochromic in type. The red cell size is normal or decreased (microcytosis), and the cells may vary strikingly in shape (poikilocytosis). The color index, mean corpuscular hemoglobin content, and mean corpuscular volume are usually less than normal. The white cell count is variable, though often elevated, and nucleated red cells may appear in the circulation if there is excessive demand on the bone marrow. The reticulocytes are increased in numbers only after initiation of adequate therapy. *The bone marrow* is usually hyperplastic. The erythroid elements are plentiful at the normoblast or erythroblast level, depending on the duration and severity of the anemia. In the severe anemias there may be also an arrest in the maturation of the myeloid elements.

These anemias respond specifically to iron. At times several preparations will have to be tried before one is found which the patient will tolerate. Ferric salts are less effective than ferrous compounds, whether organic or inorganic. The most commonly used preparations are Blaud's pills, ferrous sulfate, ferric ammonium chloride, and enteric-coated tablets of ferric salts. Occasionally, injections of inorganic iron (ferric) are necessary to produce a quantitative increase in hemoglobin[3]. The dosage of iron should be large enough to induce proper regeneration of hemoglobin. Failures in treatment are often the result of giving too little iron. In children, 0.1 to 0.3 Gm. of iron salt three times daily will suffice. In adults, the dose should be at least 1.8 Gm. a day until adequate blood regeneration has occurred. The maintenance dose will depend on the individual requirements. Crude liver extract has been used effectively in the treatment of these anemias, but refined liver extracts are of no value.

The anemia of acute blood loss does not respond specifically to iron. The treatment of this condition is control of the bleeding and the administration of plasma and blood transfusion to rebuild the blood volume. A single hemorrhage produces a leukocytosis of short duration (twelve to twenty-four hours), and an increase in platelets and reticulocytes. Recurrent bleeding may be suspected by the reappearance of leukocytosis. Iron is useful only if the bleeding is a complication of some other condition which

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has resulted in insufficient blood regeneration. The normal individual can lose 50 per cent of his hemoglobin by bleeding, and regenerate it at a rate of 1 per cent a day. He will restore his red cell values in four to six weeks and his hemoglobin values in six to eight weeks without the aid of iron.

Patients who suffer from *anemia due to chronic blood loss* (hemorrhoids, ulcerations of the gastro-intestinal tract, or polyposis) need iron. Not only do they suffer from a severe hypochromic anemia, but their hemoglobin (iron) and cell-building stores are often exhausted. It is essential to stop the blood loss. Supportive measures include transfusions of blood, and plasma transfusions are necessary when the plasma proteins have been depleted as a result of edema or the liver damaged by the long-standing anemia.

The nutritional anemias are caused by defective nutrition. This may be due to functional or anatomic alterations of the gastro-intestinal tract, or to metabolic disorders, faulty diet, or infection. These abnormalities lead, sooner or later, to a hypochromic anemia, which responds to iron. The diet is most important. If the proper food intake is assured, many of the clinical manifestations, such as glossitis and cheilosis, will disappear. Occasionally these symptoms persist despite various forms of treatment, including the administration of vitamins (riboflavin), crude liver extract, adequate diet, and iron.

Idiopathic hypochromic anemia is quite common, particularly in young and middle-aged women (usually slender brunettes). The chlorotic anemia responds specifically to iron. Hypochlorhydria is present in 70 per cent of these patients, and achlorhydria in 25 per cent[4]. The administration of dilute hydrochloric acid, 15 to 20 drops in an ounce of water by mouth fifteen minutes before meals, or of capsules containing hydrochloric acid such as acidulin, frequently relieves the gastric discomfort from which many of these patients suffer. Patients with this anemia often need iron indefinitely to maintain their health, despite an adequate diet. These women are subject to severe pelvic disorders (metrorrhagia) and may fall prey to unnecessary surgery. A few of these patients develop pernicious anemia in later life.

In vitamin C deficiency (scurvy) the anemia may be macrocytic if the patient is an infant less than 6 weeks old, or it may be hypochromic and microcytic. If it is macrocytic, it will not respond to refined liver fractions. Scurvy in infants may be due to the exclusive use of pasteurized milk or to reliance on some proprietary baby foods which lack ascorbic acid; in elderly people, particularly single men, it may be due to poor eating habits (bachelor's scurvy). The anemia responds specifically to the administration of ascorbic acid. In children 25 mg. three times daily is sufficient; adults may require 100 mg. three times a day. After ascorbic acid has been given, reticulocytosis appears. The administration of iron only enhances the regeneration of hemoglobin.

Pellagra (niacin deficiency) does not cause anemia *per se*. A few patients develop a macrocytic anemia, many more a hypochromic anemia. Nicotinic acid has no antianemic properties[5], but corrects the underlying deficiency[6]. Iron is useful to accelerate the regeneration of hemoglobin. Pellagra can be a complication of some other disease, and may develop even when the patient is receiving refined liver extract parenterally[7].

In hypothyroidism (myxedema) anemia is rather common and is usually of the hypochromic type. The bone marrow is usually hypoplastic, although few observations are available. The anemia of thyroid insufficiency may be due to defective gastric secretion, decreased appetite and inadequate diet, or it may be an attempt of the organism to adapt the hematopoietic system to the diminished oxygen requirements of the tissues. About 53 per cent of hypothyroid patients show achlorhydria. These patients need thyroid extract (1 to 5 grains a day), iron, and often dilute hydrochloric acid by mouth. Blood regeneration does not occur until the thyroid deficiency has been corrected.

In pregnancy the most common anemia is of the hypochromic type. One third of pregnant women in the first trimester and one half of women in the last trimester have red cell counts below 3,500,000. They present the usual symptoms of a chlorotic anemia (fatigue, breathlessness, glossitis, tachycardia, koilonychia). They respond specifically to iron. Many have achlorhydria, which

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requires the use of dilute hydrochloric acid. The gastric anacidity disappears in many of these women after the termination of pregnancy. The diet must of course be rich in proteins and vitamins.

In infancy a hypochromic anemia may be the result of many factors: blood loss, gastrointestinal disease, nutritional and vitamin deficiencies, metabolic disturbances, acute and chronic infections. The diet is very important. It must be remembered that milk contains little iron, and that large amounts of milk may interfere with the absorption of iron. Growth invites anemia if the iron intake is not adequate. Achlorhydria occurs in many anemic infants, but its significance is not clear. The maternal legacy is most important, since anemic mothers are unable to supply their offspring with proper stores of blood-building substances[8]. These children need iron and, in some instances, hydrochloric acid. Often this anemia can be prevented by treating the iron-deficient mother during pregnancy.

The symptoms of *hookworm disease* are due largely to the anemia. The severity of the anemia is not dependent on the number of worms which the individual harbors. Epigastric pain, abdominal cramps, vomiting, constipation or diarrhea, pallor, glossitis, abdominal distention, and arrest in growth are common. The hypochromic anemia responds to iron therapy, whether or not the parasites have been eliminated. In such cases, the eosinophilia persists.

Anemias Which Respond to Refined Liver Fractions (Soluble in 70 Per Cent Alcohol)

1. **Pernicious anemia**
2. **Sprue**
3. **Anemias of diseases of the gastrointestinal tract**
4. **Macrocytic anemia of pregnancy**

These anemias are due essentially to insufficient blood production. The *peripheral blood* fails to show evidences of a bone marrow activity which might indicate a graded physiologic response to the existing anemia. The red cells are either of normal volume or larger, and their hemoglobin content is never greatly reduced. The anemia is hyperchromic and macrocytic. Leukopenia and thrombopenia are often present. At times, the plasma contains an excess of pigment, but this is not due to abnormal blood destruction. The *bone marrow* is uniformly hyperplastic and shows a striking arrest in the maturation of the erythroid elements. Megaloblasts are abundant. This arrest in maturation of the erythroid elements can be caused by (1) lack of the extrinsic factor (B-complex derivative), (2) lack of the intrinsic factor of Castle, (3) inability to absorb the maturation factor, (4) inability to store the maturation factor, or (5) deficient utilization of the maturation factor. There are, then, many conditions which may give rise to a macrocytic hyperchromic anemia.

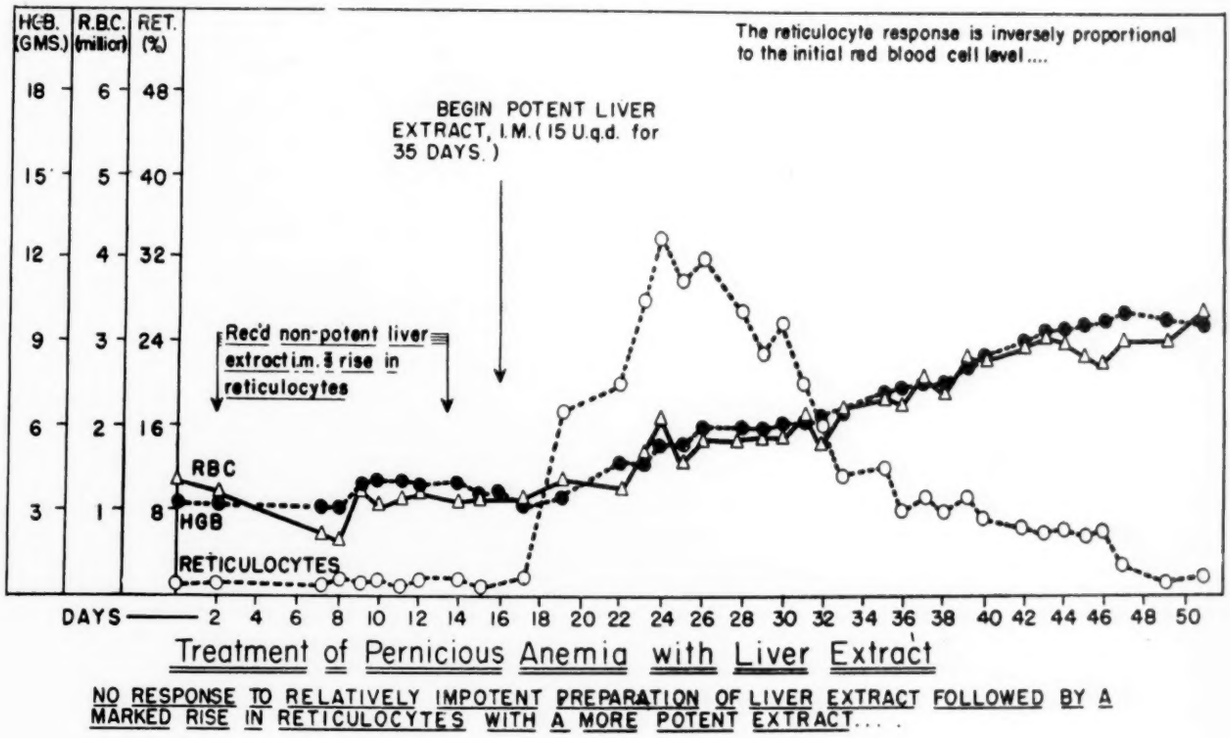
Pernicious anemia and sprue usually respond satisfactorily to treatment with parenteral extracts of liver. During the past two years, it has been found that folic acid (L. casei factor) is effective in the treatment of pernicious anemia, nutritional macrocytic anemia, and sprue[9]. We have used folic acid in 6 patients with pernicious anemia. Patients who received 30 to 50 mg. daily had a reticulocyte response comparable to that obtained with adequate doses of refined liver extract parenterally. The patients were kept on this dosage for two weeks, or until the reticulocyte peak had been passed. They then received 10 mg. daily until their red cell count had reached normal. The maintenance dose was 5 mg. daily. Although they were able to maintain their red blood cell and hemoglobin levels, the mean corpuscular volume remained above normal and macrocytosis persisted. It seems that folic acid lacks something which enables the proper liver fraction to correct completely the bone marrow abnormality. Recently it has been reported that folic acid has no effect on the neurologic complications of pernicious anemia[10]. Further observations are necessary to settle this question.

Various diseases of the gastrointestinal tract, such as cancer of the stomach or ascending colon, may interfere with the absorption or utilization of the extrinsic (hypostatic), intrinsic, or maturation factor, and lead to the development of a macrocytic anemia with a megaloblastic bone marrow. Cirrhosis of the liver or some other hepatic disease may make it impossible to store the maturation factor, so that a macrocytic anemia results. Such patients must receive refined liver fractions parenterally; oral liver

8. Strauss, M. B.: Anemia of Infancy from Maternal Iron Deficiency in Pregnancy, J. Clin. Investigation 12:345-353 (March) 1933.

9. Berry, L. J., and Spies, T. D.: The Present Status of Folic Acid, Blood, J. Hemat. 1:271-306 (July) 1946.

10. Meyer, L. M.: Folic Acid in the Treatment of Pernicious Anemia, Blood, J. Hemat. 2:50-62 (Jan.) 1947.


HGB. (GMS.)
R.B.C. (millions)
RET. (%)
The reticulocyte response is inversely proportional to the initial red blood cell level....
BEGIN POTENT LIVER EXTRACT, I.M. (15 U.q.d. for 35 DAYS.)
Rec'd non-potent liver extract i.m. & rise in reticulocytes
RBC
HGB
RETICULOCYTES
DAYS
Treatment of Pernicious Anemia with Liver Extract
NO RESPONSE TO RELATIVELY IMPOTENT PREPARATION OF LIVER EXTRACT FOLLOWED BY A MARKED RISE IN RETICULOCYTES WITH A MORE POTENT EXTRACT....

extract or folic acid by mouth is used only if the absorptive properties of the gastrointestinal tract are adequate.

During *pregnancy* a severe and even fatal macrocytic anemia may develop without obvious cause. The great majority of these patients have achlorhydria, and many lose the intrinsic factor. These patients respond, as a rule, specifically to the parenteral administration of liver extract. Some of these women have spontaneous remissions after the termination of pregnancy.

Anemias Which are Refractory to Liver Fractions, Iron, and Folic Acid

1. **Hemolytic anemias**
   - a. **Congenital hemolytic icterus**
   - b. **Sickle-cell anemia**
   - c. **Cooley's anemia**
   - d. **Erythroblastosis foetalis**
   - e. **Acquired hemolytic anemia**
     - **Malaria**
     - **Transfusion accidents**
     - **Infections**
     - **Neoplasms**
     - **Physical and chemical agents**
   - f. **Idiopathic hemolytic anemia**
2. **Non-regenerative anemias**
   - a. **Myelophthisic anemias**
     - **Chemical and physical agents**
     - **Tumor, cancer, myeloma, lymphosarcoma**
     - **Blood dyscrasias—leukemia**
     - **Aplastic anemia—marrow empty**
   - b. **Aplastic anemia—marrow full**
   - c. **Achrestic anemia**
3. **Splenic anemias**

The *hemolytic anemias* exhibit a graded physiologic response of the bone marrow. Therefore, the peripheral blood picture will be characterized by reticulocytosis, basophilia, leukocytosis, and a normochromic, usually normocytic anemia. The plasma pigments, icterus index, and urine urobilinogen will be increased. The van den Bergh reaction is indirect and the jaundice is proportional to the degree of anemia. The bone marrow is markedly hyperplastic, but there is no arrest in maturation. The treatment of these anemias varies. The congenital hemolytic icterus is favorably influenced by splenectomy, but the other forms of congenital hemolytic anemia do not respond to splenectomy.

The *splenic anemias* form a hybrid group and do not constitute a true clinical or biologic syndrome. Most cases of so-called "splenic anemia" will turn out to be instances of cirrhosis of the liver with enlargement of the spleen. The anemia is due to nutritional deficiencies, and often to blood loss from the gastrointestinal tract. Splenectomy is at times helpful, but often a risky procedure[11]. If the leukopenia is marked and the bone marrow is full, liver extract and pyridoxine may be beneficial.

11. Hanrahan, E. M., Jr.: Splenic Anemia; A Study of End-Results with and without Splenectomy Based on 35 Cases, Arch. Surg. 10:639-698 (March) 1925.

Conclusion

Anemia is rarely the result of a single factor. An anemia due to chronic blood loss may be altered and enhanced by nutritional deficiencies. The hemolytic anemias may be complicated by blood loss, metabolic upsets, and intercurrent infections, or bleeding may alter the picture of a macrocytic anemia. Hypochromic anemias are treated with iron or crude liver extract, preferably the former. These anemias do not respond to liver fractions potent in the treatment of pernicious anemia and allied conditions. The macrocytic anemias respond to these fractions, and not to iron. In some anemias with achlorhydria, dilute hydrochloric acid will allay the digestive discomfort. Some of the anemias are caused or are accompanied by a specific vitamin deficiency. This deficiency must be corrected to insure an adequate response to anti-anemic treatment. A diet rich in blood-building substances is always necessary.

THE TREATMENT OF DIABETIC ACIDOSIS

WILLIAM MCNEAL NICHOLSON, M.D.

DURHAM

Although patients with diabetic acidosis are seen with less frequency than formerly, the condition is still too common. Prevention of acidosis is the ideal goal for which the patient and physician should strive. In all cases coma is avoidable, and in most instances acidosis may be prevented. An analysis of the records of 139 patients admitted to Duke Hospital in diabetic coma[1] showed that failure to take insulin or the administration of inadequate amounts of insulin was almost invariably the precipitating factor in the production of acidosis. In some instances infection was present and the dose of insulin had not been increased to compensate for this complicating factor.

In view of the still too frequent occurrence of diabetic coma it is thought that an outline of the treatment employed at Duke Hospital for diabetic acidosis should be reported. It must be pointed out that no regimen or treatment is inflexible, but must be varied to fit each individual case. For that reason the outline of therapy is divided into three parts: (a) slight acidosis, (b) acidosis in the pre-comatose state, and (c) acidosis in coma.

Slight Acidosis

Under this heading are included patients who present the following symptoms and signs: polyuria, polydipsia, and perhaps anorexia along with malaise and drowsiness. There is usually a history of some abdominal symptoms, such as nausea and vomiting, which caused the patient to leave off his insulin. The physical examination for the most part reveals no pertinent findings; the patient is able to take and retain fluids by mouth. The urine gives a 4 plus reaction for sugar, acetone, and diacetic acid, but usually contains no albumin or casts. The blood sugar may be 300 mg. per 100 cc. or more, and the carbon dioxide combining power of the serum is not usually below 30 vols. per cent.

Obviously the therapy in this group of patients presents no great problem. However, prompt and vigorous measures must be undertaken at once. The outline of treatment is as follows:

(1) Urine and blood specimens are obtained at once. The urinary excretion of glucose and acid bodies is determined at hourly intervals, until the urine is free of acid bodies and practically clear of glucose. Determinations of the blood sugar and the carbon dioxide capacity of the serum are made at intervals of two hours until normal values are obtained.

(2) Fifty units of unmodified insulin are given subcutaneously, at once. This dose should be given in two or more sites and should be followed every hour by the administration of 25 units of unmodified insulin until the blood sugar approaches normal and a marked reduction in the urinary excretion of glucose occurs.

(3) Parenteral fluid should not be given to this type of patient. Two hundred cubic centimeters of hot broth should be given by mouth every hour. Broth made from prepared bouillon cubes contains an average of 1.1 per cent of sodium chloride. This amount is ample for the patient in slight acidosis, since 8.8 Gm. will be taken over a period of four hours. Glucose in the form of orange juice should also be given every hour, alternating with the broth. It is recommended that the broth be given every hour on the

From the Department of Medicine, Duke University School of Medicine and Duke Hospital, Durham, North Carolina.

1. Nicholson, W. M. and Branning, W. S.: Potassium Deficiency in Diabetic Acidosis, J.A.M.A., in press.

hour, and that 200 cc. of orange juice be given on the half hour. Since the carbohydrate content of orange juice averages 13.1 per cent, the patient receives roughly 26 Gm. of carbohydrate each hour.

As a rule, the blood and urine are normal or are approaching normal after four to five hours of this form of therapy. The diabetic diet and the insulin dose calculated to meet the patient's normal requirements may be started shortly thereafter.

Acidosis in the Pre-Comatose State

The prognosis in this group is usually quite good, provided adequate replacement therapy is promptly and vigorously instituted. As a rule the patient has had marked glycosuria for several days, as a result of taking inadequate amounts of insulin and indulging in dietary indiscretions. Frequently some severe infection is present and the patient has not increased his dose of insulin to compensate for it. Polydipsia and polyuria are usually present for several days and are then followed by oliguria, nausea, vomiting, somnolence and stupor. Upon examination signs of dehydration—inelasticity of the skin, dry mucous membranes, and softening of the eyeballs—may be noted. Frequently signs of shock, such as hypotension, hypothermia, and coldness of the extremities, are present. The characteristic labored respiration—the so-called Kussmaul breathing—is noted, and the mephitic, sweetish acetone breath may be detected upon entering the patient's room.

The white cells of the blood are increased in number and the blood sugar is elevated to 300 mg. per 100 cc. or more. The carbon dioxide capacity of the serum is usually less than 25 vols. per cent and may reach values of 4-5 vols. per cent. The plasma sodium and chloride are also reduced. The urine gives a 4 plus reaction for sugar, acetone, and diacetic acid, and contains albumin (approximately 1 plus); microscopically large granular casts (renal failure casts) are seen.

It is universally accepted that insulin in large amounts must be given, and that replacement of the depleted stores of fluid and electrolytes is mandatory. No general agreement on the use of alkalis and glucose has been reached[2]. The following regimen of treatment is suggested for this group of patients.

(1) Blood is obtained immediately for determination of the blood glucose and the serum carbon dioxide capacity; these tests are repeated at intervals of two hours.

(2) A urine specimen must be obtained every hour, even if catheterization is necessary. Sugar, acetone, and diacetic acid determinations are made on this.

(3) The patient is made comfortable in bed and surrounded by hot water bottles. Excessive temperature and electric pads should be avoided.

(4) Gastric lavage is done soon after the patient arrives on the ward. A small amount of normal saline (100-200 cc.) may be left in the stomach.

(5) A small, warm saline enema should be given after insulin and fluids have been started.

(6) Unmodified or crystalline insulin should be given immediately. The initial dose should be 100 units injected subcutaneously in two or more sites. This amount should be repeated at the end of one hour. The dose after the second hour depends upon the clinical improvement of the patient and the blood and urine findings. However, some insulin should be given every hour until recovery has taken place. Usually the third dose is 50 units, and each succeeding dose 25 units. If large amounts of sugar are present in the urine, the larger dose may be continued. The dose of insulin cannot be calculated in advance for any case. In our opinion the slower acting insulins are not desirable in the treatment of acidosis.

(7) The administration of fluids must be prompt. Sodium chloride in the form of normal saline solution should be started at once by hypodermoclysis in each thigh, and should be given continuously until absorption of the fluid stops, or until the patient is able to take and retain fluids by mouth. Usually 4000-6000 cc. may be given by this route.

One thousand to two thousand cubic centimeters of normal saline may be given by the intravenous route, usually at the rate of 750-1000 cc. per hour.

Glucose is usually not necessary during the first two or three hours of treatment, although we do not hold with the idea that any great harm can result from its administration, provided ample amounts of insulin are given. After the third hour of treatment

2. (a) Root, H. F.: The Use of Insulin and the Abuse of Glucose in the Treatment of Diabetic Coma, J.A.M.A. 127:557-564 (March 10) 1945.
(b) Hartmann, A. F.: Treatment of Severe Diabetic Acidosis; A Comparison of Methods with Particular Reference to the Use of Racemic Sodium Lactate, Arch. Int. Med. 56:413-434 (Sept.) 1935.

glucose should be given to compensate for the inadequate storage of glycogen in the liver, and to avert the danger of unrecognized insulin reactions. It is recommended that 1000 cc. of 10 per cent glucose be given intravenously, and that this dose be repeated in three hours if the patient is still unable to retain liquids by mouth.

Alkalis may be given in the form of sixth molar lactate. In the treatment of the *adult* we have found that the amount recommended by Hartmann[2b] is too great, since an occasional patient may develop uncompensated alkalosis. At Duke Hospital we have not found that the mortality rate is decreased by the use of sixth molar lactate. If this substance is employed, care must be exercised in interpreting the plasma carbon dioxide combining power; a high value does not necessarily reflect the true state of depletion in the patient, and vigorous therapy may be stopped short of recovery.

(8) If the syndrome of shock persists after two hours, the patient should be given a transfusion of whole blood. Usually 500 cc. are adequate, but occasionally an additional 500 cc. may be necessary.

(9) Constant observation by competent observers is essential. *The patient should never be left unattended.*

When the patient recovers sufficiently so that he is able to take and retain fluids by mouth, all parenteral fluids should be discontinued. Orange juice and broth may now be given according to the regimen outlined for patients with slight acidosis. The regular calculated diabetic diet is usually withheld for approximately twenty-four hours after the patient has recovered from the acidosis.

Acidosis in Deep Coma

We have defined the patients that fall into this group as those who cannot be aroused by painful stimulation. The history of these patients is very similar to that of patients with pre-comatose acidosis, except that the acidosis has been present longer and they have been unresponsive for several hours. The prognosis is exceedingly grave and depends upon the length of time the patient has been in coma.

Physical examination reveals all of the signs present in the pre-comatose group and, in addition, profound shock. The patients cannot be aroused from coma even by painful stimulation. The laboratory findings in the blood and urine are similar to those of the pre-comatose patients, although the changes may be greatly exaggerated. The blood sugar may be above 800 mg. per 100 cc. or may be lower than 300 mg. per 100 cc. The carbon dioxide combining power of the serum is usually around 15 vols. per cent, but it is not rare to see values as high as 25 vols. per cent. In addition to the depletion of the water from the extracellular and intracellular stores there is a great loss of the electrolytes, particularly the sodium and chloride ions, and in some patients the potassium ion. Potassium may be further depleted by the administration of insulin and fluids as outlined above[1,3].

The therapy outlined for the pre-comatose group is to be employed for these patients, the one difference being that they should receive potassium chloride. This drug should not be started until two to three hours after the beginning of treatment. If the patient at this time is able to swallow, the drug should be given by mouth every hour in doses of 0.6 Gm. until approximately 5 Gm. have been given. If the parenteral route must be followed, the potassium chloride may be given intravenously in the form of a 10 per cent solution. The initial dose should be 2 Gm. and this dose should be repeated in two hours. Where the facilities are available, the serum potassium concentration should be followed throughout the patient's recovery from coma.

3. Holler, J. W.: Potassium Deficiency Occurring During the Treatment of Diabetic Acidosis, J.A.M.A. 131:1186-9 (Aug. 10) 1946.

THE PRESCRIBING OF DIETS IN THE TREATMENT OF DIABETES MELLITUS

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An adequate dietary regimen is an essential part of good diabetic therapy. The average diabetic patient taking insulin has to keep the carbohydrate content of his meals relatively constant from day to day to avoid insulin reactions on one hand and hyperglycemia with glycosuria on the other. Well designed diets are equally important when mild diabetes is controlled by low-carbohy-

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drate diets without insulin, or by weight reduction if the patient is obese. The inability of the average physician to handle dietary problems is an outstanding cause for much slipshod diabetic treatment.

Changing Concepts of Metabolism

Recent developments in our knowledge of metabolism permit diabetic diets to be prescribed on a simpler basis than formerly. Fats are no longer thought to burn in the fires of carbohydrates[1]. It is now known that insulin deficiency simply leads to impaired oxidation of glucose. Protein and fats have then to be used disproportionately to meet caloric or energy requirements. While it has been thought in the past that 10 per cent of the fat metabolized and about half of the protein requires the use of insulin, it is now uncertain that insulin is required for the metabolism of these fractions[2]. The carbohydrate content of the diet is accordingly the principal concern in diabetic therapy. The ratio of carbohydrate, protein, and fat to one another is unimportant except as it affects the palatability of the diet. In short, there is no scientific basis for a diabetic diet other than one resembling a well selected general diet, with perhaps a moderate reduction in carbohydrate content.

Dietary Extremes

Many different plans varying in complexity and practicality have been proposed for prescribing diabetic diets and instructing the patients in their use. The old-style, weighed diets, prescribed on the basis of fixed ratios in arbitrary quantities, are still used in some quarters. While the therapeutic results are good in terms of temporary diabetic control in the hospital, lapses in treatment on the outside and outright refusal to cooperate are all too common, for patients soon discover that following a restricted and monotonous diet may be a greater curse than the uncontrolled disease.

At the other extreme are the so-called "free" diets advocated by those dissatisfied with the annoying and perhaps needless restrictions of the old regimens[3]. In some clinics where "free" diets are used all dietary restrictions have been abandoned, while in others only a few general quantitative rules are given[4]. With unrestricted diets greater degrees of glycosuria and hyperglycemia are expected and permitted, partly because they are necessary in order to avoid hypoglycemic reactions. Adequate studies of survival rates and the incidence of remote complications in patients treated in this manner have not as yet been made.

Individual Diet Prescription

Several years of experience in treating the average run of diabetic patients, as well as many with severe and unstable diabetes[5], has convinced me that individual diets are superior to all others. These diets are easily applied; they are easily understood, are pleasing to the patients who use them, and permit meticulous diabetic control.

The first step in individual diet prescription is to investigate some aspects usually ignored—the types of food available at home, the quantities desired, and the patient's likes and dislikes. From the dietary history obtained one can estimate the quantities and types of food that are practical to use. There is no point in including in a diet foods that are not available or that will not be eaten. It is ill advised to recommend radical changes in dietary habits, although adjustments may be necessary occasionally to have adequate nutrition.

All diets should contain in the day's food a pint or more of milk to provide enough calcium; fresh tomatoes, tomato juice, or a citrus fruit to supply vitamin C; two raw, green leafy or yellow vegetables; and at least 60-70 Gm. of protein. After these basic requirements are met, food items should be used in the diabetic diet according to the usual pattern set by family customs and economic factors.

The mechanics of individual diet prescription

The mechanics of individual diet prescription are made immeasurably easier if printed charts and forms similar to those illustrated are conveniently at hand. The basic foods easiest to use in a diabetic diet are the plain, simple foods of relatively constant composition, such as lean meat, eggs, milk, bread, butter, cream, fruits and vegetables. The

1. Stadie, W. C.: Intermediary Metabolism in Diabetes Mellitus, Bull. New York Acad. Med. 19:778-80 (Nov.) 1943.
2. Soskin, S., and Levine, R.: Carbohydrate Metabolism, Chicago, University of Chicago Press, 1946.
3. Tolstoi, E. and Weber, F. C., Jr.: Protamine Zinc Insulin: A Clinical Study, Arch. Int. Med. 66:670-678 (Sept.) 1940.
4. Joslin, E. P.: Diabetes Mellitus, New England J. Med. 234:476 (April 4) 1946.
5. Rundles, R. W.: Diabetic Neuropathy, Medicine 24:111-160 (May) 1945.

Table 1. Composition of Food

Food	Weight (grams)	Protein (grams)	Fat (grams)	Carb. (grams)	Calories
Egg, average size	50	6.5	6		80
Lean meat, cooked	60	18	3.6		105
Medium fat meat, cooked	60	15	11		160
Bacon, crisp	30	6	15		160
Cheese: cheddar, process	50	12	16	1	195
cottage	100	19	1	4	100
Bread, large slice	30	3	1	15	80
Crackers	20	2	2	15	85
Cereal, average portion	20	2		15	70
Milk (8 oz., ½ pt.)	240	8	9	12	160
Skimmed milk	240	8		12	80
20% cream	30	1	6	2	66
Fruit or vegetables, 3%	100			3	12
Fruit or vegetables, 6%	100	1-2		6	28
Fruit or vegetables, 12%	100	1-3		12	52
Butter, margarine	10		9		81
Salad oil	30		30		270
Cakes, angel	100	8		59	270
fruit, pound	100	6	19	53	405
Cookies, plain	100	7	15	70	440
figbars, gingersnaps	100	5	7	76	390
Dried fruit, dates, figs, raisins, prunes	100	3	1	75	320
Gelatin, plain	100	86			345
Ice cream	100	4	13	20	210
Milk chocolate	100		34	55	530
Nuts:					
Almonds	100	19	54	20	640
Brazil nuts	100	15	66	11	695
Peanuts and peanut butter	100	26	46	22	605
Pecans	100	9	73	13	740

Table 2

Outlines for individual diets varying in carbohydrate content and caloric yield. One-fifth of the total carbohydrate is given at breakfast. The noon and evening meals are equal. The quantities of food used are common amounts suitable for attractive servings. Fruits and vegetables are indicated in terms of total grams of carbohydrate from these sources per meal.

	1200 Cal. 100 C. 57 P. 68 F.		1200 Cal. 150 C. 65 P. 40 F.		1600 Cal. 125 C. 70 P. 91 F.		1600 Cal. 175 C. 72 P. 71 F.		2000 Cal. 150 C. 90 P. 115 F.		2000 Cal. 225 C. 90 P. 84 F.	
	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E
Eggs	1	2	1	2	1	2	1	2	1	3	1	3
Milk		240		240*	240	240	120	240	120	240	120	240
Bread	15	15	30	30	15	30	30	60	30	45	45	60
Butter	5	10	5	5	10	10		10	10	20	10	10
20% Cream	15				15	30	30		30	30		
Fruits and Vegetables	12	20	15	30	4	21	12	28	10	23	16	48

* Skimmed milk

	2400 Cal. 150 C. 90 P. 160 F.		2400 Cal. 225 C. 100 P. 120 F.		2800 Cal. 200 C. 110 P. 171 F.		2800 Cal. 250 C. 112 P. 150 F.		3200 Cal. 250 C. 114 P. 195 F.		3200 Cal. 300 C. 119 P. 170 F.	
	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E	Br.	N & E
Eggs	1	3	1	3	2	3	2	3	2	3	2	3
Milk	240	240	240	240	240	240	240	240	240	240	240	240
Bread	30	45	45	60	30	60	45	60	45	60	60	60
Butter	15	30	15	20	20	20	10	20	20	30	20	25
20% Cream	60	45	30	15	60	90	60	60	90	90	60	60
Fruits and Vegetables	3	21	8	46	8	32	12	54	9	52	17	74

(Br.=breakfast; N.=noon; E.=evening.)

composition of these foods, as well as that of high-calorie items less commonly allowed, is given in table 1[6].

With the general food requirements of an individual in mind, outlines of representative diets of different caloric yield and carbohydrate content can be followed as a guide in dividing the diet into meals and specific food items (table 2). The quantity of protein foods is indicated in terms of egg equivalents, and items within the protein, bread-cereal, or fatty-food groups may be interchanged freely (table 3). Unsweetened fruits and vegetables can be prescribed most easily in terms of total grams of carbohydrate from these sources per meal, the carbohydrate content being estimated from measured servings as shown in table 4[7]. This arrangement allows for the widest possible choice and variety in the diet, as well as for a proper adjustment when the choice is extremely limited—as, for instance, when

6. (a) Bowes, A. D. and Church, C. F.: Food Values of Portions Commonly Used, ed. 5, Anna de planter Bowes, 311 S. Juniper St., Philadelphia 7, 1945.
   (b) Chatfield, C. and Adams, G.: Proximate Composition of Anerical Food Materials, U. S. Dept. Agriculture Circular no. 549, 1940.
7. Diet Manual of University Hospital, Ann Arbor, George Wahr, 1945.

Table 3. Food Substitution Equivalents

Protein Foods. Substitution Equivalents for 2 Eggs.

	Wt. (Gm.)	Measure
Meat, cooked	60	2″ x 4″ x ½″
Fish, cooked or canned	60	2″ x 4″ x ½″
Bacon, cooked crisp	30	4½ strips
Cheese, cheddar, process	50	2″ x 3″ x ½″
Cheese, cottage	65	4 tbsp.
Peanut butter	30	2 level tbsp.

Bread-Cereal Foods. Substitution Equivalents

	Wt. (Gm.)	Measure
Bread	30	1 large slice
Crackers	20	5. 2″ square
Cereal: cooked (20 Gm. dry)	100	scant ½ cup
All-Bran	20	⅓ cup
Cornflakes	20	¾ cup
Grapenuts	20	⅛ cup
Krumbles	20	⅓ cup
Pep	20	⅔ cup
Puffed Rice	20	1½ cups
Puffed Wheat	20	1½ cups
Rice Krispies	20	⅔ cup
Shredded Wheat	20	⅔ biscuit

Fatty Foods. Substitution Equivalents

	Wt. (Gm.)	Measure
Butter	10	1 pat, 2 tsp.
Margarine	10	1 pat, 2 tsp.
Mayonnaise	10	2 tsp.
French dressing	15	3 tsp.
Salad oil	10	2 tsp.
Lard, bacon fat, Crisco	10	2 tsp.
20% Cream	45	1½ oz.

Name _____ Hgt. _____ Wgt. _____ Occupation _____

Diet _____ cal. _____ Pr _____ carb. Date: _____

BREAKFAST	Amount	DINNER and SUPPER	Amount	BEDTIME	Amount
Fruit or Juice		(Broth, clear soup)			
Eggs		Eggs (Meat)			
Milk		Milk			
Bread		Bread		SPECIAL FOOD SUBSTITUTES—	
Butter		Butter			
Cream		Cream			
(Coffee)		Fruit and Vegetables			
or				INSULIN DOSAGE:	
		(Coffee, Tea)		Morning Noon Night	

Chart 1. Individual Diet Instruction Card

Table 4. Carbohydrate Content of Fruits and Vegetables Estimated by Measured Servings

0 to 3 Per Cent Carbohydrate	3 Per Cent Carbohydrate	6 Per Cent Carbohydrate	9 Per Cent Carbohydrate	12 Per Cent Carbohydrate	15 Per Cent Carbohydrate	18 Per Cent Carbohydrate
Gm. Carbohydrate per serving:	⅓ cup=2 ½ cup=3	⅓ cup=4 ½ cup=6	⅓ cup=6 ½ cup=9	⅓ cup=8 ½ cup=12	⅓ cup=10 ½ cup=15	⅓ cup=12 ½ cup=18
Vegetables: Bean sprouts Beet greens Cabbage, raw Chinese cabbage Celery Chicory Cucumber Endive Escarole Lettuce Mushrooms Mustard greens Pickles, sour, dill Radishes Sorrell Spinach Summer squash Turnip greens Water cress **Fruits:** Rhubarb (This group need not be weighed or measured.)	**Vegetables:** Asparagus Broccoli Cabbage, cooked Cauliflower Chard Sauerkraut Tomatoes Tomato juice	**Vegetables:** Beans, green Beans, wax Chives Collards Dandelion greens Eggplant Kale Kohlrabi Lambsquarters Leeks Okra Pepper, green Pepper, red Pumpkin Turnips **Fruits:** Melons— Cantaloupe Honeydew Spanish Watermelon Strawberries	**Vegetables:** Artichokes Beets Brussel sprouts Carrots Onions Parsley Rutabagas Squash, winter **Fruits:** Blackberries Cranberries Currants Gooseberries Grapefruit Grapefruit juice Lemons Limes Tangerines	**Fruits:** Applesauce Apricots Cherries, sour Kumquats Loganberries Mulberries Oranges Orange juice Peaches Pineapples Pineapple juice Plums Quince Raspberries	**Vegetables:** Beans, red kidney Parsnips Peas Salsify Hominy, cooked **Fruits:** Apples Blueberries Grapes Huckleberries Mangoes Nectarines Pears	**Vegetables:** Potatoes Macaroni, cooked Noodles, cooked Spaghetti, cooked **Fruits:** Cherries, sweet Figs, fresh Grape juice Prune juice **21 Per Cent Carbohydrate** ⅓ cup=14 ½ cup=21 Beans, baked Beans, fresh lima Black-eyed peas, fresh Corn, fresh Rice, cooked Yams Bananas Prunes, fresh

the only vegetable available for a particular meal is potatoes.

As quantities adapted to the needs and preferences of a particular patient are chosen, they are entered on the individual diet card (chart 1). Absolute quantities in most cases are less important than constancy in amount and distribution of carbohydrate from day to day. The total amount of food needed is determined over a period of time by the quantity required to maintain the individual's body weight at or slightly below the optimal level.

General rules

In dealing with obese patients with gluttonous appetites, where the prescription of a reduction diet may jeopardize cooperation, it is better judgment to satisfy the food desires, maintain control of the diabetes, and allow the obesity to persist; for diabetes is a more serious disease than obesity. In the treatment of mild diabetes by low-carbohydrate diets without the use of insulin, the meals become unattractive when the carbohydrate content of a 2000-calorie diet is less than about 150 Gm., and that of a 3000-calorie diet below about 200 Gm. In some cases the patient may have to decide between less attractive food without insulin and a better diet with insulin.

Every effort should be made to avoid unnecessary restrictions in diabetic diets. Whole wheat bread, for instance, is commonly prescribed routinely. Enriched white, rye, or even hot breads, if properly estimated as to carbohydrate content, can be used equally well. The fruits and vegetables containing less than 3 per cent carbohydrate—and in many cases those through the 6 per cent groups—can be used in virtually any quantity. Black coffee, tea, lemonade made with saccharin, broth, clear soup, and average servings of oysters and clams can also be used without regard to food content. Cold lunches are easily adapted from the allowed food when desired. Bedtime lunches are usually advantageous when protamine-zinc insulin is used, and these lunches often satisfy natural desires as well.

It is important finally that the patient be made to understand the reasons for his dietary regimen, and not merely be given a set of arbitrary directives, if sustained cooperation is to be expected.

SOME COMMON FORMS OF OVERTREATMENT

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It is not the purpose of this article to discuss toxicology. It is well known that the use of drugs is attended by dangers, and physicians are keenly aware of these dangers, such knowledge being part of their training. On the other hand, prolongation of therapy often results in minor changes which are not so easily recognized or anticipated, but may do harm—not only by confusing diagnosis, but by retarding healing and return of normal function. It is with this aspect of treatment that I propose to deal by illustrative examples.

Local Treatment

Suppose that an individual is confronted by a single symptom—namely, itching. This is a very common symptom, and equally so is the usual therapy for it—scratching. In many cases this will relieve the symptom, and that is the end of it. If, however, because of lack of judgment or emotional tension or simple absent-mindedness, the sufferer continues to scratch, it may be said that he has overtreated the condition. The result will be excoriation of the skin, and the chances are that the symptom will thereby be increased rather than diminished. The sufferer may then present himself to a physician, and the diagnosis is probably not itching from the original cause—whether an insect bite or something else that may have long since healed of itself—, but traumatic dermatitis.

This easily understandable train of events illustrates the principle involved. The treatment of minor skin ailments may take other forms. Self-medication by various salves, ointments, antiseptics, and lotions prescribed by one's friends may often be prolonged to the point of slowing down and interfering with the natural healing processes of the body. One often wonders how our dermatologic colleagues are able to make diagnoses when the patient has so modified the original lesion by haphazard and prolonged topical treatment that the presenting condition is chiefly a chemical or an excoriative dermatitis.

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As an extension of the above principle, the topical treatment may have been prescribed by the physician to the patient, but he may have failed to warn him to stop it after a certain time and give the skin a chance to heal. One is inclined to assume that the patient will use good judgment, but too often this assumption proves to be a mistake.

The same principle may apply in the treatment of sore mouth. Stomatitis is a condition that may arise for various reasons: lack of cleanliness, digestive disturbances, a rough edge on a tooth, malnutrition, acute infection, the taking of unclean articles and foreign bodies into the mouth, or vitamin deficiency. The physician attempts to find the underlying cause and to treat that appropriately. There remains then to be treated the presenting symptom, a painful mouth. Commonly it is advised that a mouthwash be used. Most mouthwashes contain antiseptics, which may have irritating properties to a greater or less degree. Treatment is instituted, and the patient gets better. He frequently attributes his improvement to the local treatment, and keeps on with this. At the same time he is apt to worry with his mouth, putting his tongue here and there and feeling out the sore places to see how they are getting along. Of course his attention has been directed to his mouth in the first place, and he may be said to have a *fixation* on that part of his body. This fact must always be kept in mind in the topical treatment of any condition. In this particular case it would be far better to use a simple mouthwash such as plain water or 0.9 per cent salt solution, and to divert the patient's mind while impressing upon him the importance of not overtreating the condition.

An allied condition is herpes labialis. A common form of therapy is to apply alcohol, and this is usually successful. If the patient keeps on using it without regard to the side effects, however, he may produce a secondary condition that will give further trouble.

Laxatives

Perhaps the commonest form of overtreatment is in the matter of movement of the bowels. Deeply imbedded in our culture seems to be the necessity of moving the bowels every day. It is very hard to disabuse a patient's mind of this article of faith. It

shocks him to be told that he could go several days without having a bowel movement, although we all know that it is unlikely that any permanent harm would result. Not believing this, the patient takes a purge and has a bowel movement. He feels fine. Then —to his surprise, but not to ours—he goes for a day or a day and a half without any inclination to move his bowels. To be sure, they have been purged, and are naturally now relaxed. There is no mechanical stimulus to further peristalsis. But the fact that is uppermost in the patient's mind is that he has not had a movement. Again he takes the purge, and the same thing happens.

Further elaboration is not necessary. One clearly sees the development of a train of events: purgation, resting bowels (mistakenly called constipation), and a repeat performance. This is a clear-cut case of overtreatment due to lack of knowledge on the part of the individual. Instruction is the answer.

Nasal Vasoconstrictors

Perhaps the most fashionable form of overtreatment in the present decade is the use of nasal vasoconstrictors[1]. Prompt relief for congestion of the mucous membrane of the nose is obtained by the use of these drugs. The primary effect is vasoconstriction, and the swollen turbinates shrink down in a dramatic and gratifying fashion. Unfortunately, this primary effect is followed by a secondary vasodilatation, which is often increased by the addition of one of the sulfonamides to the solution used. Because of the relief obtained immediately after application, however, the patient tends to use the medication again and again. It has been clearly pointed out that vasoconstrictor drugs may of themselves produce a rhinitis which is indistinguishable from one due to allergy. The use of nasal vasoconstrictors undoubtedly has its place, but they must be used sparingly. When they are prescribed, it is important that the effects of prolonged treatment be kept in mind and that the patient be instructed to watch for these.

Sedatives

The importance of warning the patient that symptomatic treatment must not be continued indiscriminately may further be illustrated in the use of sedatives. Where bromides are employed, there is danger that they will replace the chloride of the body, producing serious disturbances of the skin, and of the sensorium. The latter may even become delirium. In general there is no need that these disturbances should come about. A sedative should accomplish its purpose before such a state is reached; otherwise it is clear that supplementary treatment is indicated. Often the necessity for supplementary treatment may not be apparent at the first examination, because tension is the presenting symptom. The sedative prescribed, whether bromide or one of the barbiturates, will probably relieve that symptom, but it carries the same danger as the giving of morphine to a patient with an undiagnosed acute abdominal condition: the diagnosis is obscured.

One must always regard the use of a drug as a diagnostic as well as a therapeutic procedure. Explain that a sedative should take effect promptly, but should be discontinued after a matter of four to five days. Let the patient then observe his reactions without the sedative. In many cases the tension may have been relieved by the examination and the treatment prescribed, and will not return. If it does return, a more accurate diagnosis is called for. The important thing is to instruct the patient to break the course of treatment and to observe himself, reporting to the physician any change in his symptoms. This instruction serves another purpose—that of weaning him from dependence upon the drug.

Bed Rest

The above examples serve to illustrate common forms of overtreatment. We turn now to the subject of bed rest. More and more we are becoming aware that bed rest is overdone. The treatment of acute rheumatic fever furnishes an example. This is a serious disease, and the patient must be kept in bed during the entire period of infection. It is the physician's duty to see that the evidence of infection has disappeared—that the patient has no fever and that the white blood cell count and sedimentation rate have returned to normal. Thereafter he should make it his duty to get the patient out of bed. If this is not done, the muscles

1. (a) Kully, B. M.: The Use and Abuse of Nasal Vasoconstrictor Medications, J.A.M.A. 127:307-310 (Feb. 10) 1945; (b) Feinberg, S. M. and Friedlaender, S.: Nasal Congestion from Frequent Use of Privine Hydrochloride, J.A.M.A. 128:1095-1096 (Aug. 11) 1945.

of the body, as well as the myocardium, become weakened by rest and the process of recovery is prolonged. In some cases patients have stayed in bed for years following one attack of acute rheumatic fever.

There is also evidence that the same abuse of rest is occurring in cases of heart disease in older people. Even patients with coronary occlusion should probably be gotten out of bed sooner than has been customary. Many physicians will disagree with this statement, but evidence is accumulating that it is the case. It is far too easy to make a cardiac invalid out of a person by keeping him in bed too long.

The entire subject of the abuse of bed rest was discussed in a symposium on therapy recently[2]. It was pointed out that the bed as a therapeutic device is usually taken for granted, and that insufficient consideration is given to the dangers of going to bed. Prolonged confinement in bed is in direct conflict with physiologic principles. It creates problems. The effect on morale is not the least important one, and the patient who "looks longingly at a chair" should probably be allowed to use it. There are gastro-intestinal problems—distention, and the common objections to the bedpan. Backaches and muscle cramps result from abnormal pressure when the patient is in bed. There are pulmonary and circulatory problems—the latter particularly in patients with heart failure[3].

This group of physicians, in discussing the subject, pointed out that sitting in a chair quietly is as effective as lying in bed in many cases, and that patients are often less restless. The particular problem of coronary thrombosis was brought up. In general a minimum of six weeks in bed is prescribed, but there seems to be considerable doubt that even this is always necessary. Except in the most acute phase of the disorder, the greater freedom of sitting in a chair might materially improve the condition of the patient. The formation of thrombi in the veins of the legs is one of the more serious complications of bed rest. When one is forced to prescribe bed rest, he should not forget that moving the legs with reasonable frequency may prevent this serious complication.

2. On the Use and Abuse of Bed Rest. Cornell Conferences on Therapy, vol. 1, New York, The Macmillan Company, 1946.
3. Harrison, T. R. et al.: Symposium on the Abuse of Rest in the Treatment of Disease, J.A.M.A. 125:1075-1092 (Aug. 19) 1944.

Conclusion

No doubt every physician is aware of the types of overtreatment touched on in this paper. Many more instances could be cited, and no doubt each reader will bring to mind some particular example. The principles involved are in general the same, although in the case of bed rest there are unusual dangers, and it is here that the judgment of the physician is most important in deciding what is best to be done. The experienced practitioner learns to consult with the patient in making these decisions, and this is a good course to follow. The inclination of the individual is not lightly to be disregarded.

As for the overenthusiastic use of drugs, the physician's judgment of the personality of the patient using the drug is here the touchstone. The sensible person will not indulge in overtreatment, while the too dependent individual will tend to cling to the drug prescribed by the physician. It is better to err on the side of overinstruction than to assume that the patient will use good judgment.

Physicians are often warned to remember that they are treating sick human beings rather than a disease. It is well to recall here the words of Withering: "It is much easier to write upon a disease than a remedy. The former is in the hands of nature and a faithful observer with an eye of tolerable judgment cannot fail to delineate the likeness; the latter will ever be subject to the whims, the inaccuracies and the blunders of mankind." Fashion and publicity modify and are responsible for various types of treatment. They do not prevent the effects of overtreatment; indeed, they may serve to increase their incidence.

Summary

Most therapeutic measures are double-edged swords; they can do harm as well as good. Prolonged use is one of the ways in which harm may be done. Some common examples of this form of overtreatment are discussed.

For centuries, scratching an itch has been one of the pleasures as well as a curse of humanity. One of the King Georges of England is credited with the statement that "only kings should have the itch, since it is such a kingly pleasure to scratch." While the psychic background of pruritus is well known, the mechanical, bacterial and chemical stimuli to itching are more frequent. But the diagnosis pruritus without limiting or descriptive additions is still good form, even a necessity in many instances.—Herbert Alden and Jack W. Jones: Neurodermatitis, Am. Practitioner 1:152 (Nov.) 1946.

THE SIGNIFICANCE OF HYPERSENSITIVITY IN DIAGNOSTIC TESTS AND IN THE THERAPY OF INFECTIOUS DISEASES

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The importance of hypersensitivity in asthma, hay fever, and tuberculosis is recognized by all physicians. The clinical syndromes of asthma, hay fever, and urticaria result entirely from the explosive reactions of certain tissues to materials which are harmless to the normal individual. Such a pattern of reactivity, which is not only useless but actually harmful to an allergic patient, is closely related to the basic mechanism of immunity which protects man from extinction when he is infected by pathogenic bacteria, viruses, or fungi.

Types of Antibody Reaction

Serum sickness is a classic example of a disease in which all the clinical manifestations result from a too-rapid production of antibodies by the immune mechanism in its effort to eliminate the offending foreign protein from the body of the patient. Some individuals succeed in producing antibodies and in eliminating the foreign serum without developing symptoms. Such a type of reaction is obviously the most desirable for the patient, and is analogous to a subclinical infection in which the infecting agent is eliminated without the development of symptoms and yet resistance is acquired to subsequent infections with the same pathogenic organism.

A few individuals[1] seem to lack the ability to produce antibodies to horse serum; the foreign protein circulates in the blood for months, and serum sickness does not develop. In such instances the failure to eliminate the horse serum by antibody formation is not dangerous, because the serum itself is harmless and gradually disappears. However, if such an individual were infected with a living virus or bacterium, he probably would succumb quickly to the infection because of his inability to produce antibodies.

Thus, the clinical manifestations following the parenteral introduction of foreign serum into the human body can be classified as follows: (1) the normal, or moderate, reaction; (2) the hypersensitive reaction; and (3) the hyposensitive reaction. In the normal, or moderate, reaction, antibodies are produced, the foreign serum is eliminated, and few, if any, symptoms appear. In the hypersensitive person antibody is produced in quantity and the foreign serum is eliminated, but the patient becomes violently ill in the process. In the hyposensitive patient few, if any, antibodies are produced; there is no conflict between antigen and antibody, and serum sickness does not occur. In any series of cases all gradations from hypersensitive to hyposensitive reactions may be observed.

In naturally acquired infectious diseases of man, the problem is much more complicated than in an artificially produced disease such as serum sickness. In natural infections, the foreign protein is a part of a living, multiplying virus, bacterium, fungus or parasite, and the disease is complicated further because some of the infecting agents secrete exotoxins and others contain endotoxins. In many instances, however, the hypersensitive reactor can be detected and the course of his disease can be modified by desensitization.

Before discussing practical methods of desensitization we must return again to our study of serum sickness. In most instances of serum sickness, whether subclinical or clinical, the tissue cells of the body after recovery are altered in such a manner that a second injection of the same foreign serum results in new symptoms, characterized by an onset which is sudden and often violent. The intravenous injection of the specific serum may produce an anaphylactic type of reaction, while the subcutaneous or intramuscular injection of the same material may result in the actual necrosis of tissues—the "Arthus phenomenon." On the other hand, the injection of 0.1 cc. of a 1:10 dilution of the serum intradermally produces in the next twenty to thirty minutes an urticarial wheal which disappears within half an hour, leaving no evidence of injury. Such a skin test, harmless in itself, is valuable in that one can predict which patients would

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1. Longcope, W. T., and Mackenzie, G. M.: The Relation between the Disappearance of Foreign Proteins from the Circulation and the Formation of Antibodies, Proc. Soc. Exp. Biol. & Med. 17:133-136, 1920.

react violently to large doses of the same serum injected intravenously or intramuscularly. Furthermore, a positive skin test indicates that, at some time in the past, the patient has had a clinical or subclinical case of serum sickness.

In contrast to the immediate intradermal reaction indicating previous contact with *serum*, there is another type of reaction to protein which is seen only in patients who have had previous *infections*. In both cases the injected material is harmless to those who have had no previous contact with the specific protein. The delayed types of reaction differ from the immediate in that the tissue cells at the site of the skin test are damaged or destroyed. This destruction of body cells due to tissue hypersensitivity should not be confused with the destruction of body cells by direct action of toxin, as is seen in the Schick test.

Although the immediate and delayed types of skin reaction develop under quite different circumstances and although there are marked differences in the mechanisms by which they are elicited, the mechanisms are similar enough so that the physician can be guided by the same general principles in his management of all patients who react in an unusual manner to infecting organisms. Thus, there are hyper-reactors, moderate reactors and hypo-reactors to infectious agents, and, as in serum sickness, the clinical symptoms differ in different patients, even though they all were infected with the same organism.

Diagnostic Skin Tests

There are a number of specific diagnostic skin tests in use which depend upon this principle of specific hypersensitivity of the tissues to the protein of the infecting organism. Among these are tuberculin for tuberculosis, mallein for glanders, brucellergin for brucellosis, histoplasmin for histoplasmosis, coccidioidin for coccidioidomycosis, tularense deaminized bacterin for tularemia, and various bacterial and fungus vaccines. The Frei test is an example of an allergic reaction to a virus infection. Of diagnostic importance also is the immediate type of skin-test reaction seen in certain parasitic diseases such as trichinosis. It should be emphasized that a positive skin test does not prove the presence of active disease. A previous infection, clinical or subclinical, may so greatly sensitize the tissues that a positive skin test may be elicited for many years. This knowledge is of major importance in the study of patients suspected of having brucellosis. Since a positive skin test itself will frequently give rise to agglutinins and increased phagocytosis within a few days, blood should be drawn for agglutination and phagocytic studies before the skin test is performed, to avoid a false conclusion that the patient has active brucellosis.

The Moloney test, while not a diagnostic test for infection, is important practically as a test for individuals who are hypersensitive to diphtheria toxoid[2]. Schick-positive individuals who have negative Moloney tests (0.1 cc. of a 1:100 dilution of fluid toxoid) can be given full doses of the toxoid without fear of local or general reactions. Moloney-positive individuals can be rendered Schick-negative by three to six intradermal injections, at weekly intervals, of the toxoid diluted 1:100—that is, by repeated Moloney tests[2].

Some Effects of Hypersensitivity

The increasing local and general reaction to repeated doses of typhoid vaccine is probably another example of hypersensitivity. This problem may be solved by employing small (0.1 cc.) doses of the vaccine intradermally[3].

Recurrent herpes may be an example of hypersensitivity to a virus, analogous to recurrent boils due to staphylococci. Vaccination with vaccinia virus usually gives a marked reaction after twenty-four hours, and repeated vaccinations may desensitize the patient and eliminate the recurrent herpes.

The development of hypersensitivity during the course of an infection may be one of the reasons for the chronicity of certain diseases (tuberculosis and fungus diseases), and may account for the persistence of symptoms in some individuals infected with organisms which cause acute infections in the moderate reactor. The development of hypersensitivity apparently counteracts the effectiveness of the immune bodies, possibly

2. Bunch, C. P., Morrow, R. C., Jr., Timmons, J. R. and Smith, D. T.: Studies on the Immunization of Adults with Diphtheric Toxoid, J. Immunol. 39:427-440 (Nov.) 1940.
3. (a) Perry, R. M.: Comparison of Typhoid "O" and "H" Agglutinin Responses Following Intracutaneous and Subcutaneous Inoculation of Typhoid, Paratyphoid A and B Vaccine, Am. J. Hyg. 26:388-395 (Sept.) 1937.
   (b) Martin, Donald S.: Intracutaneous vs. Subcutaneous Vaccination, North Carolina M. J. 3:492-495 (Sept.) 1942.

by interfering with the phagocytic mechanism. Recurrent boils frequently respond readily to an autogenous, or even a stock vaccine. Chronic infections of the nasal sinuses, bronchi and lungs, if not conditioned by local mechanical factors, often improve with autogenous vaccines; the hypersensitivity factor should be proved by preliminary skin tests.

One of the best examples of the effect of hypersensitivity in modifying the course of a disease is the hypersensitive type of chronic brucellosis, where the patient is clinically ill, but shows a good titer of agglutinins. Although antibodies are present, sometimes in abundance, they apparently are not effective in eliminating the infection. Such patients have little or no phagocytosis, but strongly positive skin tests to brucellergin. Desensitization with brucellin apparently decreases the hypersensitivity enough to allow the already existing immunity to become effective[4].

4. Smith, D. T. and Poston, Mary A.: Some Unusual Cases of Brucella Infection, Tr. Am. Clin. & Climat. Assoc., 1937.

DESENSITIZATION IN THE TREATMENT OF ASTHMA

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There are many phases in the treatment of asthmatic patients. Most reports deal with the symptomatic relief of an attack. Adrenalin, aminophyllin, and the newer antihistamine preparations such as benadryl and pyribenzamine provide the physician with an armamentarium which, when judiciously used, will relieve the paroxysm of dyspnea promptly. Since asthma is noted for its chronicity and recurrence, more effort should be devoted toward preventing the attacks. The attitude that patients "outgrow their asthma" or that it will subside spontaneously is not justified and is not in keeping with sound medical practice. The sooner asthma is accepted as a serious, disabling disease and is put in the category with pernicious anemia and diabetes, the better the condition will be controlled.

Types of Asthma

Two general types of asthma are encountered. In one there are recurrent paroxysms of cough, wheezing, and dyspnea—the typical asthmatic attack. These attacks usually come on suddenly and, when treated successfully, subside; the patient remains asymptomatic between the paroxysms. The other type of asthma is seen in those patients who may not have enough respiratory distress to require emergency relief but who stay "wheezy" and short of breath day in and day out. These patients often develop complications of emphysema, bronchitis, bronchiectasis, and pulmonary fibrosis sooner than those with irregular but more severe paroxysms.

There is a general attitude among the laity that nothing can be done for asthma. This attitude accounts for the fact that, all too often, patients with asthma do not seek medical advice for many years. When they are first seen, emphysema, diminished vital capacity, and chest deformity are already established. Treatment at this stage can only arrest the process at best, and the patient is left with a permanent pulmonary insufficiency.

It is true that some cases of asthma seem to defy all therapeutic efforts, but such cases are certainly in the minority. Statistics are notoriously unreliable in allergic diseases, because the course is unpredictable and there is no objective method to determine the efficacy of treatment[1]. As more patients are studied thoroughly and given a systematic course of treatment, the failures will become fewer.

Every asthmatic patient is entitled to a thorough medical and allergic work-up. Protein sensitization tests, when correlated with the history, are invaluable in establishing the causative factors. Once the etiology is established, the therapeutic program can be outlined. Patients with asthma are usually cooperative in carrying out a plan of treatment, if the logic of such a plan is explained to them. From the patient's standpoint there is nothing more discouraging, after being subjected to a detailed history and physical examination and numerous skin tests, than to be dismissed with a casual statement that "nothing much was found," or to be given a long list of foods to avoid, or advised to stay clear of dust. The majority of such patients have already discovered that dust

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1. Levine, Philip and Coca, A. F.: Studies in Hypersensitiveness. XXII. On the Nature of the Alleviating Effect of the Specific Treatment of Atopic Conditions, J. Immunol. 11:449-464 (June) 1926.

causes trouble and have taken measures to control it. *There is no practical way to avoid entirely the inhalant allergens which are largely responsible for asthma.* The logical treatment is (1) to avoid exposure to the offending substances as much as possible, and (2) to lessen the sensitivity which has been acquired.

Desensitization

Asthma is basically a disease of hypersensitivity; therefore, efforts should be directed toward decreasing this sensitivity. Rarely is an allergic individual found to be sensitive to only one or two substances. As a rule, there are multiple sensitivities[2] to environmental factors which cannot be avoided unless the patient is forced into a very abnormal existence.

Desensitization is the process by which an antigen is repeatedly introduced in increasing amounts until fairly large doses can be tolerated without producing allergic symptoms. The mechanism of desensitization differs from that of immunization. In the latter, the antigen is given to stimulate the production of antibodies to protect the body against a biologic invasion; in the former, the antigen is given in very small amounts to neutralize existing antibodies.

Various routines are used for the desensitization of an allergic individual. Perennial, pre-seasonal, and co-seasonal methods all have their advocates. Specific desensitization is preferred when the etiologic agent is known.

Determination of the patient's sensitivities

A thorough medical and allergic investigation is essential to determine the agent or agents involved. Skin-testing gives much information in a short period of time, but should always be correlated with the history. Positive reactions to fall pollens mean little when the asthma occurs in the winter or spring.

Advantages of the intradermal method of skin-testing are that the results are quite uniform and that a large number of tests can be given in a short time. Serious reactions are very rare. Among thousands of patients tested in the Duke Clinic, each receiving from 100 to 150 separate tests at a sitting, no serious reactions have been encountered. However, serious and even fatal reactions to skin tests have been reported, and adrenalin should always be available for immediate use. The reactions are read in fifteen to twenty minutes.

When the history is suggestive of bacterial sensitization, a bacterial vaccine is prepared from the sputum or nasopharyngeal secretion. Skin tests to the individual organisms grown on culture may reveal positive reactions to one or several among the group.

General principles of desensitization

Practically all standard textbooks on allergy recommend desensitization in the allergic diseases, but to outline a workable plan for every case is difficult. In asthma there are usually multiple allergens, and the results of treatment are not uniform. The number of allergens to include in the mixture, the strength of the initial dilution, the method of administration (hypodermic, intravenous, oral), the frequency of injection, the rapidity of increase, and the length of time treatment should be continued are problems which must be decided in each individual case. There are four essential rules to follow in any program of desensitization:

1. *Prepare a solution containing the major reacting allergens.* There is no reason why extracts of pollens, dust, danders, molds, a few foods, and a bacterial vaccine cannot be made into one solution. This method simplifies the program a great deal.

2. *Begin with a solution that will not cause local or systemic reactions.* In general, the pollens, dust, danders, and certain of the foods are potent allergens and have to be used in more dilute solution than the molds and bacterial vaccine. For diagnostic intradermal testing this clinic uses the pollens, dust, and epidermals in a 1:1,000 dilution, foods and molds in a 1:100 dilution, and bacteria in a 1:10 dilution and undiluted (24-hour growth from agar slants washed into 30 cc. of saline). There are some exceptions where the dilution has to be adjusted to prevent false-positive reactions.

3. *Progressively increase the dose until a fairly concentrated solution is being given without reaction.* As the amount of allergens is thus increased, a tolerance is acquired, and clinical improvement usually parallels this acquired tolerance.

4. *Maintain the patient's tolerance by continuing the injections at regular intervals.* Usually a course of treatment lasts six to

2. Cooke, R. A. and Vander Veer, Albert, Jr.: Human Sensitization, J. Immunol. 1:201-305 (June) 1916.

twelve months, and the patient is then re-evaluated and re-tested to see if any sensitivities have been lost or any new ones acquired. If symptoms persist and new sensitivities are discovered, subsequent courses of treatment are given.

Method of desensitization

Serial dilutions of the reacting allergens are prepared in vials of saline, provided with rubber stoppers to prevent contamination. Injections are given subcutaneously with a tuberculin syringe, which facilitates the measurement of small doses. *The treatment should be carried out in a systematic and uninterrupted manner under the supervision of a physician.* Our routine is to begin with an initial dose of 0.1 cc. of the weakest dilution and to increase the dose by 0.1 cc. at each subsequent injection — either every other day or twice weekly. When the dose of 0.9 cc. has been reached, the next strongest dilution of the mixture is used. Each dilution is administered in the manner described above. This schedule is continued until the dose of 0.9 cc. has been reached in a fairly concentrated solution with the allergens in a 1:25 dilution, fungi 1:10 and the autogenous vaccine undiluted. Five tenths cubic centimeter is then given weekly as a maintenance dose.

The following is an outline of a typical desensitization schedule:

Three to four months may be required before a fairly concentrated solution can be given without reactions. After 0.9 cc. of the fourth dilution is reached, the dose is reduced to 0.5 cc., and this amount is given weekly for seven or eight months. The whole course of treatment extends over a period of ten to twelve months. It is helpful in keeping records if the physician will fill in the date when each of the injections is given.

Results

Evaluation of the results of treatment in asthma depends entirely upon clinical observation and the length of time the patient remains improved. The word "cure" does not have a place in the prognosis of asthma. Relapses are frequently seen in patients thought to be "cured," if they are followed long enough. The problem, therefore, is one of controlling a condition which tends to relapse. It would not be over-optimistic to say that two thirds of the patients who complete the outlined desensitization schedule get good results. Best results are obtained when the asthma is largely due to extrinsic factors. Desensitization with the inhalant allergens is uniformly more effective than bacterial desensitization. However, bacterial vaccines[3] have frequently given good results

3. (a) Walker, I. C.: The Treatment of Bronchial Asthma with Vaccines, Arch. Int. Med. 23:220-234 (Feb.) 1919.
(b) Crump, Jean: Asthma in Children Treated with Autogenous (Bronchoscopic) Vaccine, Am. J. Dis. Child. 58:768-777 (Oct.) 1939.

First dilution	—	Allergens*	1:20,000	**Third dilution**	—	Allergens	1:200
		Fungi	1:4,000			Fungi	1:40
		A. V.†	1:2,000			A. V.	1:20
Date:				Date:			
.....		0.1 cc.		.....		0.1 cc.	
.....		0.2 cc.		.....		0.2 cc.	
.....		0.3 cc.		.....		0.3 cc.	
.....		0.4 cc.		.....		0.4 cc.	
.....		0.5 cc.		.....		0.5 cc.	
.....		0.6 cc.		.....		0.6 cc.	
.....		0.7 cc.		.....		0.7 cc.	
.....		0.8 cc.		.....		0.8 cc.	
.....		0.9 cc.		.....		0.9 cc.	
Second dilution	—	Allergens	1:2,000	**Fourth dilution**	—	Allergens	1:25
		Fungi	1:400			Fungi	1:10
		A. V.	1:200			A. V.	Undiluted
Date:				Date:			
.....		0.1 cc.		.....		0.1 cc.	
.....		0.2 cc.		.....		0.2 cc.	
.....		0.3 cc.		.....		0.3 cc.	
.....		0.4 cc.		.....		0.4 cc.	
.....		0.5 cc.		.....		0.5 cc.	
.....		0.6 cc.		.....		0.6 cc.	
.....		0.7 cc.		.....		0.7 cc.	
.....		0.8 cc.		.....		0.8 cc.	
.....		0.9 cc.		.....		0.9 cc.	

*Pollens, other inhalants, and foods.
†Autogenous vaccine.

in cases where there is no active focus of infection.

Causes of poor results or failures in treatment are:

1. *Stopping treatment too early.* If the patient improves rapidly, he is inclined to discontinue treatment. If there is no noticeable improvement for several months, discouragement is inevitable.

2. *Interruption of treatment schedule.* There are many factors which operate here, negligence probably being the most common.

3. *Continuation of contact with allergens.* The tolerance achieved by desensitization is only a relative one. Exposure to large quantities of the offending allergens may exceed the patient's threshold of tolerance. An offending food may be at fault when the symptoms persist in spite of treatment.

4. *Failure to discover all factors responsible for symptoms.* It is impossible to test a patient to every substance which can cause asthma. Common environmental allergens are used, plus additional ones indicated by the history. Skin tests are by no means infallible, and a negative skin test does not rule out any particular substance.

5. *Active foci of infection.* The problem of controlling a bacterial allergy is difficult if there is any active focus of infection in the upper respiratory tract.

6. *Situational reactions.* Asthma may be a convenient disease for some. The disease may be serving a purpose which makes the patient reluctant to part with it.

PENICILLIN AEROSOL THERAPY

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The use of penicillin and other antibiotics as aerosols for the treatment of certain pulmonary infections is a logical procedure, simple to perform, and one that frequently gives good results. Some time ago, one of us[1] reported on the topical application of penicillin in infections of the nose, mouth, and throat. At that time we tried to find a simple method whereby patients might actually inhale penicillin. The breathing of penicillin as a spray made by an ordinary atomizer was a failure in our hands, despite a recent article to the contrary[2]. The particles of liquid were apparently too large, and, despite numerous attempts, we never felt that in a single case we were able to coat the pulmonary tract with the drug. Many articles[3] during the past ten years have emphasized the importance of the inhalation of bronchial dilators for asthma, and it seemed obvious that in these cases the drug did enter the bronchial tree. That penicillin could be made to enter the bronchial tree and to be absorbed from the lungs into the circulation has been amply proven by Barach[4] and Segal[5].

Method of Treatment

After some experimentation, it was found that a simple apparatus manufactured by the Vaponefrin Company, with the trade name of "Complete Vapocillin Equipment," was quite satisfactory. This equipment essentially consists of a vaporizer which is attached to a nosepiece or a mouthpiece, and a re-breathing bag. In order to vaporize the solution, a gas or air under pressure is required. For the treatment of hospitalized patients, we have most frequently used the ordinary oxygen tank with a reduction or flow valve. With the reduction valve adjusted to about 2 pounds of pressure per square inch, or the flow valve adjusted to deliver from 6 to 18 liters of oxygen per minute, approximately twelve minutes are required to vaporize 1 cc. of antibiotic. Flow valves or the usual oxygen equipment is difficult to obtain, and we have found that a common reduction valve, such as is used in commercial work, does just as well as the more expensive equipment. A simpler source of power is obtained by the use of a small, electric-driven air compressor, like that used for a paint-spray gun. The cheapest and simplest method so far discovered to give the necessary pressure is an ordinary foot-operated automobile tire pump.

One cubic centimeter of penicillin is usually

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1. Menefee, E. E., Jr., and Atwell, R. J.: Effect of Topical Penicillin on Infections of the Upper Respiratory Tract, South. M. J. 39:726-728 (Sept.) 1946.

2. Morse, F. W.: Penicillin Spray by Bulb Atomizer in Respiratory Infections, J.A.M.A. 132:272-278 (Oct. 5) 1946.

3. Richards, D. W., Jr., Barach, A. L., and Cromwell, H. A.: Use of Vaporized Bronchodilator Solutions in Asthma and Emphysema, Am. J. M. Sc. 199:225-232 (Feb.) 1940.

4. Barach, A. L. et al.: Inhalation of Penicillin Aerosol in Patients with Bronchial Asthma, Chronic Bronchitis, Bronchiectasis and Lung Abscess, Ann. Int. Med. 22:485-509 (April) 1945.

5. Segal, M. S. and Ryder, C. M.: Penicillin Aerosolization in the Treatment of Serious Respiratory Infections, New England J. Med. 233:747-756 (Dec. 20) 1945.

administered at each treatment. The strength of the solution may be varied, but, in our opinion, it should never contain less than 10,000 units. Perhaps 20,000 or 25,000 units per cubic centimeter is preferable in most cases. We believe that treatment should be given at least four times a day. The dose of streptomycin is much less certain, but probably 250,000 micrograms four times a day is not too great. Since it is well known that many bacteria rapidly develop resistance to streptomycin, it is better to overtreat, despite the present high cost of the drug, than to take a chance on giving too little of this antibiotic.

Results of Treatment

Up to the present time we have treated 87 patients for various pulmonary infections.

Laryngitis

Six patients with acute catarrhal laryngitis were treated. All had a history of coryza or sore throat preceding the laryngitis, but in most of these the earlier symptoms had disappeared, and at the time of admission they were complaining only of a dry, burning sensation of the throat and marked hoarseness. Physical examination showed little of interest. On indirect laryngoscopic examination, the vocal cords were found to be hyperemic and swollen. All patients were put to bed and told not to talk, and penicillin aerosol was started. Within twelve hours, or after three treatments, there was marked subjective improvement in every case. By the end of forty-eight hours all traces of acute inflammation had disappeared.

Acute tracheobronchitis

Eleven patients with acute tracheobronchitis in which the predominating bacterial agent was a streptococcus, pneumococcus, or staphylococcus were seen and treated. Seven of these had histories of preceding colds, while in 4 the onset was acute without any previous symptoms. In no case did the temperature exceed 38.5 C. (101.3 F.). Physical examination was negative in all cases except for the usual signs of upper respiratory infection. Careful examination of the lungs revealed some fine rales over the bases, bilaterally; x-rays of the chest were normal, however.

These patients were treated with penicillin aerosol, in the manner described above, and within five days all were apparently cured. Most of them felt much better within one day, with marked diminution of cough and disappearance of the dull, substernal discomfort. Three other patients, who showed primarily Micrococcus catarrhalis in their sputum cultures, did not show definite improvement after three days of penicillin aerosol therapy. Hence this therapy was discontinued and sulfonamides by mouth were substituted, with better results.

Chronic bronchitis

A total of 14 patients were treated. The average duration of symptoms prior to aerosol therapy was seven months, and every patient had been treated by other methods. Nine patients were cured or greatly improved by aerosol therapy; 3 were temporarily improved, while 2 showed no improvement. Brief summaries of 3 cases will best illustrate the results.

Case 1

M.T., a 55-year-old white female, was admitted on July 26, 1946, complaining of chronic cough, purulent sputum, and low-grade fever with general malaise. These symptoms were of eight months' duration. She had been treated with autogenous vaccines, sulfonamides, parenteral penicillin, steam inhalation, and various cough syrups without improvement. Physical examination revealed rales at both bases. She raised an average of 30 cc. of purulent sputum per day. Sputum cultures showed Staphylococcus aureus, beta hemolytic Streptococcus, and alpha hemolytic Streptococcus. She was started on penicillin aerosol, 20,000 units four times a day. After two days the cough was much less severe, and after six days of treatment she ceased to raise any sputum. Treatment was continued for a total of twelve days, and the patient was then discharged. She has been frequently seen as an outpatient since, and has had no return of symptoms.

Case 2

L.H., a 37-year-old white female, was admitted on August 14, 1946. She had had a chronic cough for two years. Physical examination showed numerous rales and rhonchi in the lower half of both lung fields. Bronchograms were done and were entirely normal. No infection in the upper respiratory tract could be found by the otorhinolaryngologist. She was started on penicillin aerosol, 20,000 units four times a day. There was marked improvement in her condition, with disappearance of cough, clearing of the physical signs, and reduction in the amount of sputum. After ten days of therapy, she was discharged as improved. Within three weeks, however, she had a return of symptoms and has had to be treated repeatedly at home. Hence she is classified as only temporarily improved.

Case 3

E.M., a 30-year-old white male, was admitted on August 18, with a diagnosis of chronic bronchitis of eleven months' duration. Physical examination showed little of interest except for rales at both bases. X-rays of the chest were entirely normal. He was treated with 25,000 units of penicillin aerosol, administered four times a day for fourteen days.

At no time did he show any definite improvement. He is therefore classified as unimproved.

Bronchiectasis

Once dilatation and deformity of bronchioles have taken place, it is obvious that no medical therapy can ever correct the pathologic process. Surgical removal of all diseased portions of the lung is the only possible cure. On the other hand, there are many patients with bronchiectasis who for various reasons are not suitable candidates for surgery, or who absolutely refuse operation. In such cases penicillin aerosol has proven to be of value in the control of bronchiectasis. Ten patients who were not suitable candidates for resection were treated with penicillin aerosol. Six were definitely improved, while 4 did not show any reduction of symptoms.

The 4 patients failing to show improvement ranged in age from 36 to 64, and the duration of symptoms varied from three to fifteen years. Three had bilateral involvement; 1 had extensive unilateral bronchiectasis. In 3, the sputum contained the usual flora that would be expected: staphylococci, streptococci, and fusospirochetal organisms. These 3 patients were treated with 20,000 units of penicillin four times a day for a minimum of twelve days. At the end of that time there had been no diminution of cough, the sputum was not decreased, and the same organisms were still present on sputum culture. It is possible that the dosage of penicillin was entirely too small, the frequency of treatment insufficient, and the duration of treatment too short. The fourth patient showed numerous colonies of Friedlander's bacillus on sputum culture, in addition to Staphylococcus aureus hemolyticus. When he failed to improve on penicillin aerosol, he was tried on streptomycin aerosol, receiving 0.25 Gm. four times a day for five days. This also failed to produce any noticeable improvement.

The 6 patients who showed definite improvement on penicillin aerosol varied in age from 20 to 66 years. Their symptoms had been present for a minimum of one year and a maximum of thirty years. The sputum of these patients varied in amount from 30 cc. to 150 cc. a day, and contained the usual flora. These patients received 20,000 units to 25,000 units of aerosol penicillin four times a day for ten to twenty days. At the end of the course of treatment, 5 of the 6 had no sputum at all, while in 1 case the sputum had decreased from 80 to 20 cc. per day. They all felt better, had little or no cough, and were gaining weight. After discharge from the hospital they have continued to be improved, although with upper respiratory infections they temporarily become worse. Several have their own equipment and continue to treat themselves at home for an average of seven days out of each month. Two return to the hospital from time to time for further treatment.

Seven patients with bronchiectasis who were suitable candidates for operation were treated from three to ten days prior to surgery. In each case the sputum was decreased in amount and became less purulent in character. They all stood the operative procedures well, and are symptom-free at present. It is the opinion of the thoracic surgeons that preoperative therapy is of distinct benefit. In one patient, a 23-year-old male who had had bronchiectasis for at least fifteen years, it was decided to remove the left lower lobe, which showed extensive bronchiectatic changes by bronchogram. Minimal changes were also present in the right lower lobe. Following operation he continued to bring up some purulent sputum. Penicillin aerosol therapy was then begun, and all symptoms and sputum disappeared. By the judicious use of aerosol from time to time, he has remained symptom-free and has been able to return to work.

Pneumonia

Seven patients with bronchopneumonia have been treated with penicillin aerosol alone. These ranged in age from 17 to 42 years. None were extremely ill on admission to the hospital, but the diagnosis was confirmed by x-ray in all cases. Sputum cultures showed the common organisms: pneumococci, staphylococci, and streptococci. All showed rapid subjective improvement, were afebrile within forty-eight hours after therapy was started, and were discharged from the hospital in less than a week. We have not treated any cases of pneumococcal lobar pneumonia by penicillin aerosol. Although Segal[5] has shown that this disease can be successfully treated by penicillin aerosol, we feel, as he does, that it is simpler and more efficacious to treat pneumococcal lobar pneumonia by the sulfonamides or by parenteral penicillin. Two patients with atypical pneumonia, probably virus, were treated with

penicillin aerosol. As would be expected, there was no evidence of improvement in either case.

Lung abscess

Seven patients with lung abscess were treated with penicillin aerosol. In 4 patients, none of whom had had the process more than ten weeks, there was rather prompt diminution of the sputum and the temperature became normal after three to six days. Serial x-rays showed the surrounding pneumonic process to clear within ten days, and by the end of the third week no cavity was visible. The patients were discharged from the hospital on modified bedrest, a high-calorie diet, accessory vitamins, and sulfonamides to be taken at home. They have been followed in the outpatient clinic for periods of three months to one year, and so far all have remained well.

One patient with multiple cavities in the right upper lobe, who had been sick for four months, was treated for seven days with 25,000 units of aerosol four times a day. At the end of this time he had shown no improvement, and was actually worse. Aerosol was continued, and parenteral penicillin given also. He still failed to improve and, after a second week, was transferred to surgery. The right upper lobe was removed, and the patient then made an uneventful recovery.

Two other patients with lung abscesses were also treated with penicillin aerosol. They showed subjective improvement, and x-rays showed clearing of the surrounding pneumonia. At the end of nineteen days of treatment, however, the cavities were still present. They were transferred to the surgical service, where open drainage was instituted in one case, and lobectomy was performed in the other. Both patients are now apparently well.

Intrinsic asthma

Nine patients with intrinsic asthma were treated with penicillin aerosol. Their ages varied from 21 to 64 years. The usual history revealed no seasonal incidence in the asthma, but showed that it always occurred following upper respiratory infections. On admission they were all having acute asthmatic attacks which started off with coryza, followed by a cough with purulent sputum, and then by bronchial spasm. Seven patients were markedly improved after four to nine days of aerosol therapy. In one of these, benadryl was given in addition to the aerosol, and another received aminophyllin suppositories. Five patients, however, received penicillin aerosol alone. In all patients who showed improvement, sputum cultures and autogenous vaccines were made, and at the time of discharge from the hospital they were started on the usual desensitization program, to be carried out for the long-range therapy.

Two patients did not improve. One was a 55-year-old white male whose asthmatic attack had been going on for sixteen days prior to admission. He received 20,000 units four times a day for ten days, and at the end of this time he still had all of his symptoms. The other, a 48-year-old female, seemed slightly worse after five days of therapy, and penicillin was discontinued.

Friedlander's bacillus infection

Four cases of Friedlander's bacillus infection were treated with aerosol, with varying results.

Case 1

E.M., a 29-year-old white female, was admitted to Duke Hospital complaining of cough and fever of ten days' duration. X-rays of the chest showed a patchy, confluent bronchopneumonic process in the right lower lobe. Sputum cultures showed large numbers of Friedlander's bacilli. The patient was started on streptomycin aerosol, 0.25 Gm. in 1 cc. of normal saline, receiving this dose four times a day. After four days, her temperature was normal, and by the sixth day, x-rays showed the process to be clearing rapidly. The patient has remained well.

Case 2

A.M., a 50-year-old male, was admitted complaining of asthma of seven days' duration. X-rays revealed a pneumonic process in the right upper lobe. Sputum cultures showed Friedlander's bacilli to be the predominating organism. He was given 0.15 Gm. of streptomycin aerosol four times a day for seven days. After the third day the bronchial spasm was relieved, and at the end of the seventh day x-rays of the lungs were clear.

Case 3

A.P., a 47-year-old female, was admitted complaining of chronic, recurrent cough, purulent sputum, and frequent hemoptysis of fifteen years' duration. Bronchograms showed bilateral bronchiectasis. The sputum was cultured, and a pure growth of Friedlander's bacillus resulted. She was treated with 25,000 units of penicillin aerosol four times a day for nine days without improvement. She then received 0.25 Gm. of streptomycin eight times a day for three days. At the end of this period, neither the cough nor the sputum had improved. For the next fourteen days she received 1 cc. of aerosol containing 0.33 Gm. of streptomycin and 40,000 units of penicillin four times a day. There was still no change, and the patient was discharged unimproved.

Case 4

B.D., a 50-year-old male, was admitted with recurrent, intrinsic asthma. X-rays showed the lungs

clear. Sputum cultures grew Friedlander's bacilli, alpha Streptococci, Neisseria sicca, and an anaerobic mixture. No streptomycin was available, and he was treated with penicillin aerosol, 20,000 units four times a day for ten days. At the end of that time there had been no subjective improvement, and repeated sputum cultures constantly showed the same organisms.

Miscellaneous conditions

Seven patients with miscellaneous infections or diseases of the respiratory tract were treated, with indifferent results. One patient with lipoid pneumonia received penicillin aerosol, 20,000 units four times a day for seven days, without any improvement. One patient with interstitial fibrosis of the lung of unknown etiology received aerosol penicillin, 25,000 units four times a day for ten days. At the end of that time his cough, sputum, and shortness of breath were no better. One patient with tuberculosis of the trachea received 30,000 units of penicillin aerosol for sixteen days, with no improvement. Unfortunately, because of the excessive cost, streptomycin could not be tried. Successful treatment of a somewhat similar case with streptomycin has been reported[6]. Three patients with monilia infection of the lung received aerosol therapy for an average of ten days each. X-ray showed no real change at the end of this time, although 2 patients felt better and had less sputum. One patient with bullous emphysema and superimposed bronchitis was treated for ten days with penicillin aerosol. At the end of this time his cough was much reduced, his sputum had completely disappeared, and his shortness of breath was markedly relieved. X-rays showed no change, however, and it is obvious that the improvement was due entirely to the clearing of the bronchitis. As would be expected, the emphysema was not affected.

Summary

Eighty-seven patients with various infections of the respiratory tract have been treated with penicillin or streptomycin aerosol. In the acute bacterial infections, such as laryngitis and acute tracheobronchitis, penicillin aerosol seems to reduce the length and severity of the disease. In many cases of chronic bronchitis of long duration, aerosol therapy gives temporary or permanent improvement. Cases of bronchiectasis, not suitable for surgery, can frequently be controlled by the use of penicillin aerosol, although it is obvious that there is no permanent improvement and that such patients need rather frequent courses of treatment. Acute lung abscesses are apparently helped by aerosol therapy, although in the more chronic cases the results are disappointing. Intrinsic asthma seems to be helped in a large percentage of cases, but this method of treatment should not be substituted for desensitization therapy.

Streptomycin used as an aerosol gives definite promise of being of great benefit in certain of the gram-negative bacterial infections of the respiratory tract. Virus diseases, fungus diseases, and diseases due to chemical agents or of unknown etiology are not affected by penicillin or streptomycin aerosol.

Conclusion

The antibiotics given in the form of aerosol offer a simple therapeutic approach to many of the common diseases of the respiratory tract. The equipment necessary to carry out such treatment is not too expensive, and it can be easily used at home. Further study of this approach, particularly with the use of the newer antibiotics, should be carried out.

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NEW HORIZONS IN DRUG THERAPY

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The ultimate aim of most medical practice is the treatment of disease or the correction of abnormal states in the body. Much of this treatment is accomplished by the administration of chemicals, which we choose to call drugs. For centuries most of these drugs were crude mixtures, usually given empirically with the most fanciful theories as to their mode of action, and often with severely depleting effects upon the patient. However, since the establishment of the modern science of pharmacology and the application of laboratory methods to the study of drugs, progress in medical treatment has been relatively rapid.

It is beyond the scope of this paper to review all of the numerous recent advances in drug therapy, but attention will be directed to some of those which have particular sig-

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nificance for the future. Among the most spectacular achievements of modern science have been the new antibacterial drugs. With the development of these compounds it has become increasingly apparent that drugs may act upon bacteria in ways which are basically similar to the mode of action of therapeutic agents in man. This basic similarity is in the regulation of physiologic processes in the organism, whether microbe or man. In dealing with disease-producing micro-organisms it is our purpose so to influence these processes that growth of the invaders becomes impossible.

"Competitive Inhibition"

It has been learned, at least in part, how this purpose is accomplished by sulfanilamide, and at the same time information of great value in understanding drug actions and in pointing the way to new developments has been obtained. It was discovered quite early that extracts of tissues, yeast, and bacteria could inhibit the antibacterial action of sulfanilamide. Further study revealed that this inhibitory effect was due to the presence of para-aminobenzoic acid (one of the constituents of the vitamin B complex), and that the effect could be produced in the test tube or in animals by the synthetic chemical. It then was found that para-aminobenzoic acid (PABA) is necessary for the growth of many bacteria—an "essential metabolite." Sulfanilamide and PABA are closely related in structure, and it is believed that sulfanilamide prevents the growth of bacteria by taking the place of PABA in the chemical reaction in which it normally is concerned in the growth of organisms. In this way the utilization of the essential metabolite is prevented by sulfanilamide (a "competitive inhibitor"), so that metabolism and growth are halted[1].*

The situation is quite complex[2], and only a beginning has been made in the study of the principle of metabolite antagonism or competitive inhibition. However, compounds have been produced which interfere with the utilization of chemically related essential metabolites by micro-organisms and animals. A striking example is furnished by dicoumarol and vitamin K. These substances possess chemical similarities, and in all probability dicoumarol decreases the prothrombin of the blood (and hence its coagulability) by competing with vitamin K in its essential role in the synthesis of prothrombin. Also it now appears quite likely that the occurrence of nicotinic acid deficiency in animals on a corn diet (and perhaps of pellagra in man) is due to the presence of a "competitive inhibitor" of nicotinic acid in corn[3]. Further understanding of the principle of competitive inhibition almost certainly will open new horizons in the development of drugs. For instance, little is known concerning the mode of action of the antibiotics, but it is not unlikely that some phenomenon such as that described above is concerned in their antibacterial effects. Progress has been made in the difficult chemistry of these compounds by the synthesis of penicillin[4], and we may anticipate that further knowledge will lead to better remedies, as well as to other fundamental advances in chemotherapy.

It should be pointed out that some of our older drugs exert their effects by competing for active receptors on cells or in enzyme systems, thus preventing the attachment of the usual chemical mediator or metabolite. Such drugs as curare and atropine, which block certain body functions, probably act in this way. In other instances drugs stimulate to action certain structures, such as muscle or gland cells, by attaching themselves to the receptors of those cells, thus simulating the effect of the normal chemical mediator. Space does not permit further development of this subject, but it is of the greatest importance in understanding and anticipating the action of drugs.

It can be seen from the above discussion that "chemotherapy" and "drug therapy" are merging in the fundamental concepts of the action of chemical substances on cells and vital processes. As these concepts are more clearly elucidated, they serve as guide posts for the discovery and synthesis of new drugs which constantly extend our horizon, not

*Space does not permit the mention of all important publications pertaining to the subjects discussed in this paper. Therefore references cited are not necessarily the earliest papers, but often are later articles which furnish a more complete bibliography. Apology is made for omissions which have occurred in this way.

1. Welch, A. D.: Interference With Biological Processes Through the Use of Analogs of Essential Metabolites, Physiol. Rev. 25:687-715 (Oct.) 1945.
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3. Woolley, D. W.: The Occurrence of a "Pellagragenic" Agent in Corn, J. Biol. Chem. 163:773-774 (June) 1946.
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only in therapy, but also at times in the understanding of disease.

Chemotherapy of Infections

The chemotherapy of infections had its beginning with the arsenicals of Ehrlich, but the advances made in the comparatively few years since the discovery of sulfanilamide have been spectacular, to say the least. With the synthesis of newer sulfonamides and the discovery of penicillin, the field of protection has gradually broadened, and now includes two of man's traditional enemies—cholera and plague—to say nothing of the spirochetal diseases. Furthermore, streptomycin now promises to bring under control many virulent infections due to gram-negative bacilli, such as tularemia; and the trial of streptomycin and the sulfones in tuberculosis and leprosy may be regarded as preliminary to a concerted attack upon those diseases. Much also has been accomplished in the field of chemotherapy of protozoan infections, such as malaria and tropical diseases[5], by the synthesis of new compounds.

However, as potent as the above chemotherapeutic agents are against certain organisms, they are ineffective in most of the diseases due to fungi, rickettsiae, and viruses. There is promise from experimental work[6] that an antibiotic with fungistatic properties may be developed in the not-too-distant future. Rickettsiae and viruses, unlike bacteria, grow inside cells, instead of extracellularly. Apparently because of this intracellular growth, they have different metabolic processes from bacteria. The most encouraging results in the control of these intracellular organisms have been obtained with the rickettsiae.

Sulfonamides do not inhibit the growth of these organisms in culture[7], and in fact it has been reported that such drugs actually have a harmful effect in experimental typhus[8]. The above considerations, together with the knowledge that sulfonamides inhibit the metabolism of para-aminobenzoic acid (PABA) by bacteria, led to the trial of PABA on rickettsiae. The results were striking in that this substance, which is necessary for the growth of many bacteria, has a strong inhibiting effect on the growth of rickettsiae[9]. The laboratory studies have been extended and confirmed in clinical medicine by the trial of PABA in typhus, spotted fever, and scrub typhus[10], with beneficial effects. Thus, through studies growing out of sulfonamide research, PABA has assumed a position of great physiologic and therapeutic importance. With such momentous gains behind us, it is not unreasonable to expect that chemotherapy of even the virus diseases eventually will become a reality.

Regulation of Body Processes

Autonomic nervous system

It has been pointed out above that drugs may be thought of as producing their effects by regulating physiologic processes in the body. The greater the number of these processes we can control by drugs, the more versatile becomes the science of therapeutics. Many of these vital processes are regulated by the autonomic nervous system, and many of our drugs exert their effects by increasing or inhibiting the effects of the sympathetic or parasympathetic division upon the organs innervated. We have potent drugs for increasing the effects of either division, such as mecholyl and prostigmine for the parasympathetic, and adrenalin and ephedrine for the sympathetic division. We also have, in atropine, a fairly satisfactory agent for lessening the activity of the parasympathetic nerves. The greatest deficiency in the field of autonomic drugs, however, has been the lack of a usable compound to inhibit the effects of sympathetic nerves. Interesting and potentially valuable drugs for this purpose now are in the experimental stage—so-called adrenolytic and sympatholytic agents. One of these, priscol, has been found to produce beneficial effects in Raynaud's disease[11]. Experiments which we have performed on animals have confirmed earlier reports concerning this drug, and some encouraging preliminary results have been ob-

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tained in patients with vasospastic states[12].

Cellular growth

It would be most helpful to be able to control the process of cellular growth in the body when this growth becomes abnormal in malignant neoplastic diseases. Among the great mass of research which is under way in the study of these diseases, not the least important is the searching inquiry into the intimate chemical nature of malignant tissue. If specific chemical affinities can be discovered, it may be possible to design radioactive chemical substances which will carry irradiation directly to the malignant cells, as radioactive iodine has been reported to do in metastatic carcinoma of the thyroid[13]. In this instance the specific affinity of thyroid tissue for iodine made possible this approach.

A new group of war gases, the nitrogen mustards, have been found to have significant effects in retarding cellular growth, especially upon lymphoid and similar tissues[14]. These effects are exerted chiefly on cells which are in a state of relatively rapid proliferation, thus resembling the effects of x-ray. Results with the clinical use of two of these drugs in certain malignant diseases have given promise of their being of value, especially in Hodgkin's disease and lymphosarcoma[15]. Our experience with one of the nitrogen mustards at Duke Hospital[16] has been in accord with the published reports. This new field is largely unexplored, however, because there are many such compounds yet to be subjected to study.

Central nervous system

We have little knowledge of how drugs regulate the functions of the central nervous system. One of our greatest needs is for drugs which will relieve pain, but will not produce addiction. We are handicapped by lack of understanding of the action of such drugs as morphine on the central nervous system. Demerol has been of great value, especially because of its spasmolytic properties and because there is less danger of addiction with its use. However, that danger still is present[17], and the physician who doubts this fact is apt to have it demonstrated to him among his own patients. Research on analgesic drugs has been stimulated by the recent discovery of a number of compounds prepared in Germany[18], and it is to be hoped that valuable remedies will be found among these or other synthetic substances. An interesting new concept of the action of chemicals on the higher centers, which can only be mentioned here, is the use of lactic acid in the treatment of certain depressive mental disorders[19].

Excretion of substances from the body

Often situations arise in which it is desirable to regulate the excretion of some substance from the body—usually to hasten the excretion of some undesirable substance. This effect often may be accomplished by freeing the material from a combined state in the body, or by regulating the elimination of the compound by the kidney. The use of diuretics to rid the body of excess fluid is an example, as is the increase in excretion of uric acid produced by salicylates and cinchophen.

BAL (British Anti-Lewisite) is a compound of great value which hastens the excretion of poisons such as arsenic and mercury[20]. It was developed during the recent war as an antidote for one of the most-feared was gases, Lewisite—an exceedingly toxic arsenic compound. BAL seems to have great affinity for arsenic, and forms a harmless compound with the poison, so that it is excreted, instead of combining with vital cellular enzymes.

Occasionally our purpose is best served by retarding the excretion of a substance—penicillin, for example. One of the chief drawbacks of this drug is the rapidity with which it is lost in the urine. It has been found that, at usual plasma levels, penicillin is excreted largely by "secretion" through

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the renal tubules[21]. Simultaneous administration of other substances which are eliminated through the tubules will reduce the rate of excretion of penicillin by overloading the excretory mechanism[22]. This method is not practical, however, because such large quantities of the other substances are required. Recently it has been suggested that the transport of penicillin through the tubule cells, from blood to urine, is due to enzyme action, and that it should be possible to block this enzyme system by a "competitive inhibitor." The preliminary report indicates that the loss of penicillin in the urine can be greatly reduced by a chemical which is said to fulfill this hypothesis[23]. Much study is necessary, but if this concept can be developed into a workable method it may revolutionize the administration of penicillin.

There are other developments in the control of body processes by drugs which offer new and rapidly expanding opportunities in therapy. Control of the clotting mechanism of the blood, regulation of the production of thyroid hormone, and prevention of the harmful effects of histamine may be mentioned as examples which cannot receive further attention at this time. It also has been demonstrated in recent years that by no means all of the advances in therapeutics depend upon the discovery of new drugs. Both sulfanilamide and penicillin were known for years before their value was realized. There is no estimating the possibilities of compounds now known, which have not received careful study. For instance, curare, which for years was a pharmacologic curiosity, now has assumed great importance in anesthesia and other fields[24].

Conclusion

It is obvious even from this limited survey of advances in therapy, achieved and anticipated, that the physician will find it difficult to keep abreast of the rapid developments and to utilize them wisely, scientifically, and with due regard to the safety of his patients. This responsibility is a staggering one, and to cope with it the physician must be properly prepared by his training in medical school and in the teaching hospital. He must be made to realize early in his career that if he is to keep up with medical progress he must have basic training in the fundamental medical sciences which will enable him to *understand* and *evaluate* new developments as they occur.

In the broad sense, physiology is the basic science of medicine; and pharmacology, which deals with the regulation of physiologic processes in man or in his microbe enemies by drugs, is the foundation of medical therapeutics. The practicing physician cannot be expected to be an expert in these fields, but he must be taught, and frequently reminded, of the habits of thought which will enable him to analyze the problems confronting him in the light of the underlying pathologic physiology of disease and the application of the pharmacologic action of drugs to those problems. This type of thinking must be applied not only to the effectiveness of drugs, but also to their dangers. For instance, the failure of some physicians to understand the simple facts that sulfonamides, when taken into the body, must be excreted largely through the kidneys and that they are liable to precipitate in the urine if precautions are not taken, resulted in many serious renal complications from the use of these drugs.

Only by utilizing and cultivating this approach will the physician (and his patients) reap the greatest benefits (and the fewest dangers) from the rapid strides in medical treatment. As Soma Weiss, one of the great teachers and investigators of modern medicine once wrote, ". . . in . . . therapeutic problems, 'skill' and 'art' are but the summation of rational clinical analysis (diagnosis) and synthesis (treatment)."

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Maternal Welfare Section*

INDUCTION OF PREMATURE LABOR

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During the course of a pregnancy it may become necessary, in the interest of the mother or the fetus, to consider termination of the pregnancy. If this procedure is adopted, it should be clearly understood that the doctor is directing the course of events and has estimated and justified his position. It should also be recognized that the labor is apt to be different from a normal spontaneous labor, the correct term being "induction of premature labor." Induction of premature labor should not be carried out as a matter of convenience; it must have a basis of factual necessity. Once elected, it may progressively build into a major "obstetric headache" by consecutively calling for more and more interference.

Methods of Induction

There are two methods of induction of labor—medical and surgical. Naturally, everything being equal, the simpler and less dangerous should be elected. This is the *medical* method. Once the necessity for the induction is proven, the indications met, and the contraindications ruled out, the following procedure is followed: The patient is hospitalized and allowed breakfast. She is then given a tablespoonful of castor oil and, an hour later, a simple warm enema. While the enema is retained, 2 minims of pitocin is given hypodermically (the patient naturally being on a bedpan). If uterine contractions supervene, no more injections are given. If no pains develop, the pitocin (minims 2) is repeated every half hour until labor begins, or for not more than eight doses. Mathieu and Homan have employed this method in a large series, and reported good results, provided the course is rigidly supervised. If the induction fails, the patient is allowed twenty-four to forty-eight hours' rest, and the procedure is then repeated. The incidence of failure with this method is about 10 per cent.

Investigators in Detroit have shown that the blood level of "pituitrin" varies in different individuals. The trend is toward an increase in the latter weeks of pregnancy. On the basis of this finding they advise increasing the dosage of pitocin by 1 minim at each successive attempt to induce labor, stopping at 8 or 10 minims. Hospitalization is essential because of the necessity of close and constant observation. If tetanic contractions, "painful pain," or evidence of placental separation or fetal distress is noted, immediate sedation and anesthesia are needed.

Some obstetricians prefer the use of castor oil alone, but we have not found this method uniformly effective. Quinine was once extensively used to increase uterine contractions, but the bulk of evidence shows conclusively that there is danger of producing congenital deafness and other distressing sensitivity phenomena in both the mother and child.

If the second medical attempt results in failure and immediate induction of labor is necessary, one should consider *surgical or mechanical* methods. Again one should select the simplest method—in this instance, the rupture of the membranes. The preliminary procedure, as outlined by Hillis, is manually to force the head into the pelvis, to check the fetal heart, and then to determine by rectal examination that the head will "fit" into the pelvis. Anesthesia is not required. An aqueous antiseptic is used, since the patient is not asleep. Strict aseptic technique should be observed. The vaginal tract should not be invaded more than once by the examining fingers. The simple expedient of "stripping" the membranes from the cervix while evaluating the consistency and degree of dilatation of the cervix further insures success of the procedure, at the same allowing "forewater" to form. The rupturing instrument is carried along the examining fingers, and the membranes are encountered and ruptured. After rupture the area is palpated to determine if the cord or an extremity has prolapsed. It is our opinion that the latent period varies inversely with the amount of fluid evacuated, but we do not advocate displacing the presenting part in order to facilitate evacuation of the fluid. A quantity of the antiseptic is poured into the

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vagina, and the fetal heart immediately checked.

Labor usually results within one to twelve hours following such a procedure. We have discarded bougies, catheters, and packs as unnecessary. We rarely use a conical bag. It fails to produce effacement while effecting dilatation, and often, in an effort to save the fetus, we have had to resort to immediate version and extraction in instances where prolapse of the cord is associated with removal of the bag. This procedure is much more difficult when the cervix is poorly prepared.

Indications for Induction

In the interest of the mother

Certain diseases incidental to pregnancy and previously existing diseases aggravated by pregnancy may occasionally require induction of labor. The most important of these indications are the *late toxemias of pregnancy* and their complications. These have been discussed in preceding articles published by the Maternal Welfare Committee. De Lee insisted that the diagnosis of an acute nephritis made in pregnancy should call for interruption of the pregnancy. The consensus supports this position. We feel that the hazard to the future health of the mother is in direct ratio to the length of time such complications are allowed to exist. Within reason, and with the patient's and husband's consent, we terminate such complicated pregnancies. Of course we hope to carry the pregnancy until the viability of the fetus is assured, but no one can promise a living baby in a toxemic mother. Too often when this hope is pursued and interruption delayed, the fetus dies *in utero*, or an already crippled kidney is seriously damaged. When the mother has nephritis, it is necessary that the family be acquainted with the possible outcome and be allowed to share the responsibility of a continued pregnancy. In this complication the obstetrician's hand may be forced by the appearance of painful vaginal bleeding, since approximately 50 per cent of the cases of ablatio placentae occur in toxemic patients. Under such conditions termination of pregnancy is urgent.

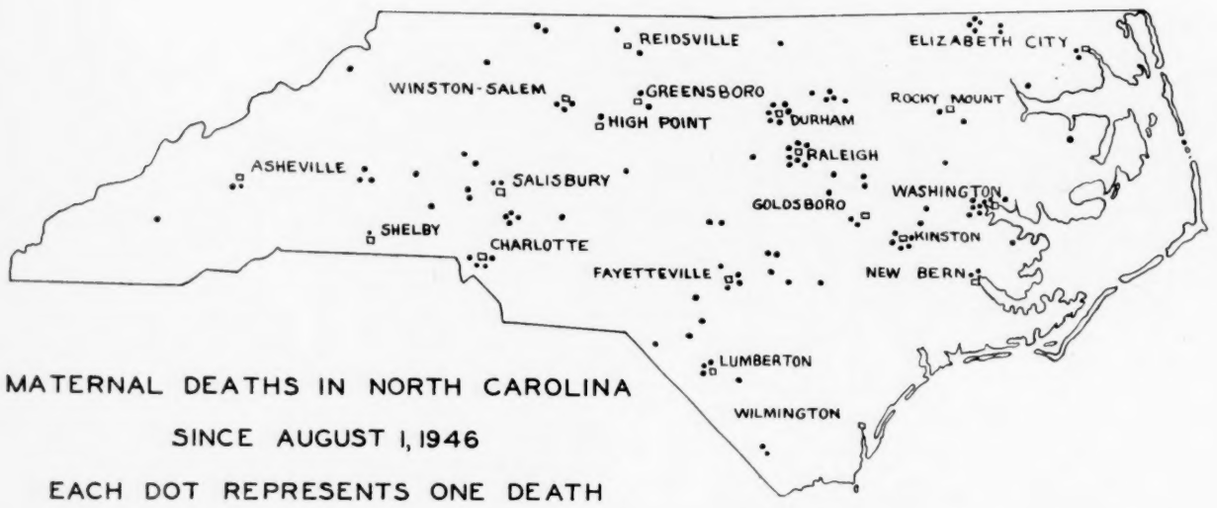
In patients with *eclampsia* it is necessary first to get the eclamptic state under control. The intake and output of fluids should be approximately equal, the circulation should be stabilized, the nervous system rested by sedation, and sources of infection corrected before labor is induced. Toxemic patients are more liable to shock and infection; therefore repeated attempts at medical induction should be made before rupture of the membranes is done. We believe that these patients go into labor more easily than normal patients, but we are apprehensive of a latent period after mechanical interference.

Accidental hemorrhage (premature separation or abruptio placentae) in the last trimester has been mentioned, but painless bleeding from varying degrees of *placenta praevia* is more frequent and really more compelling, since the chance of fetal salvage is greater. The diagnosis may be made by the history, external findings, and "soft tissue" x-ray. If this evidence is not conclusive, the patient should be examined vaginally by the aseptic technique. It is wise to have everything ready to institute immediate measures for terminating pregnancy if the examination precipitates troublesome bleeding. One may rupture the membranes, use Willett's clamp on the presenting part, insert a Voorhees bag, use pitocin, or even deliver the patient by version or hysterotomy if the cervix permits. This problem is more properly discussed in next month's article on "Hemorrhage in the Last Trimester."

There is some valid controversy as to whether labor should be induced in women with *constitutional diseases*, just as there is over the question of performing elective cesarean operations in such patients. In the past the diseases most frequently under consideration were pulmonary tuberculosis, diabetes, heart disease, thyrotoxicosis, and debilitating diseases. These conditions shall be considered in order.

In the proper handling of the tuberculous patient one must lean heavily on the internist's opinion. The consensus is that interruption of pregnancy and induction of premature labor are rarely indicated. If proper care and caution are exercised during pregnancy, the mother's life is not shortened nor the infant's safety jeopardized.

The Joslin group in Boston advocate cesarean section in the diabetic patient. It is a moot point whether such patients are apt to become toxic and whether the infant may be oversized or may perish *in utero* or soon after delivery. Some believe that labor should be induced. Our experience is against rou-



tine induction of labor or routine hysterotomy. If the labor is closely supervised and medical consultation obtained, the mother and child should survive.

If a patient with heart disease is allowed to become pregnant, she can in all probability be carried to term and normal delivery effectuated. The one notable exception is the patient who has cardiac decompensation during pregnancy. If compensation is restored, I would be inclined to induce labor during a favorable period, rather than take chances on a second breakdown. In some instances it may be difficult to decide between induction of labor and the alternate method of delivery, hysterotomy.

All of us have seen patients who do not tolerate pregnancy and who have some inherent or acquired quality which appears to make their condition more critical as pregnancy progresses. Such a patient may have to have her pregnancy terminated by induction of labor. The woman who has had large babies with resulting birth injuries, and the woman who has previously had difficult and prolonged spontaneous labor may benefit by induction, especially if they have had a repair operation that has given relief.

In the interest of the fetus

The welfare of the fetus naturally shares consideration with that of the mother. The object of any pregnancy is to produce a normal, living infant and a physiologically and psychologically adjusted and competent mother. Quite often the attainment of the latter objective depends on the former. It is a recognized fact that a mother who has a normal, healthy baby is more apt to have a normal postpartum course. One must remember that infants delivered after induction of premature labor are apt to be immature or premature, and the necessary preparations must be made for the reception and care of such infants. Such preparation is especially necessary for children delivered of toxic mothers, who perhaps constitute the largest group of women requiring this procedure.

In the mother who has had repeated stillbirths or death of the fetus *in utero* in the latter months of pregnancy labor may be induced prematurely in the hope of delivering a healthy fetus. The procedure may be carried out for the same reasons in the mother who has had an unusually large baby.

With increasing knowledge of the Rh factor and erythroblastosis fetalis, one should be alert for the possibility of incompatability. Where there is an increase in the mother's titer of anti-Rh agglutinins, especially in the latter months of pregnancy when the child is viable, one may consider the possibility of inducing labor in the interest of the fetus.

Under most circumstances one must remember that there is a choice of methods, and that the welfare of both mother and child should be considered in the selection of the procedure to be followed.

Contraindications to Induction

Experience suggests that some of the pitfalls and contraindications to induction of labor should be mentioned. Do not surgically induce labor in patients with monsters, hydrocephalic, or acephalic infants. Spontane-

ous labor with proper operations, sometimes destructive, when the cervix is fully dilated is more satisfactory in an otherwise thoroughly unsatisfactory circumstance. Death of the fetus *in utero* is not an indication for induction of labor. Distressing results—infection occurring during the latent period, and crippling of the mother—often occur when pressure by the patient, the family, and neighbors force the harassed doctor to induce labor. Such patients will ultimately go into spontaneous labor, which will be attended by fewer complications.

Summary

In summary, the patient should be carefully examined, her history studied, and any contraindication evaluated. Then, when one is satisfied that the indications warrant it, labor should be induced by one of the methods described.

THUMBNAIL SKETCHES OF EMINENT PHYSICIANS

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OBSTETRICS AND GYNECOLOGY IN AMERICA

III

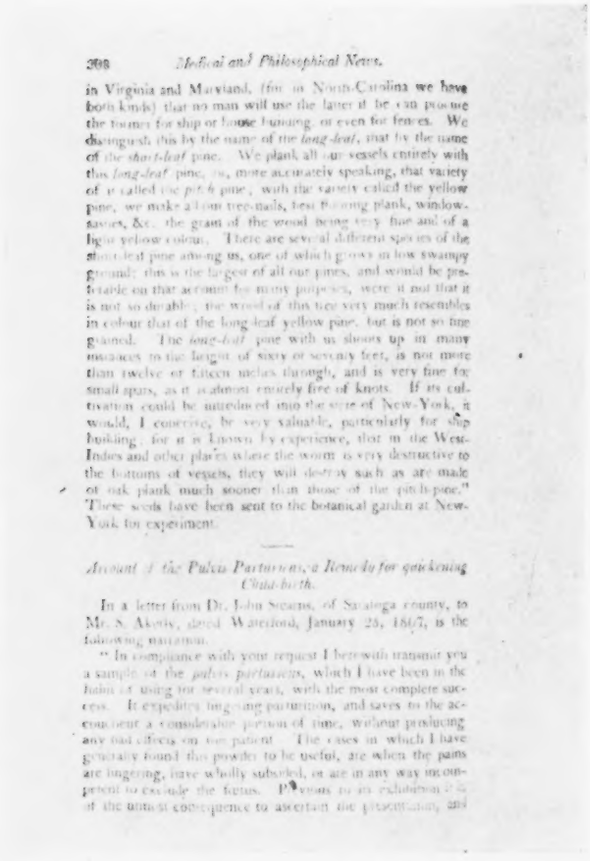
JOHN STEARNS, 1770-1848

"St. Anthony's fire" was one of several names applied in the middle ages to a terrible disease which appeared among the poor of Europe. It came in two forms: the gangrenous, in which the limbs rotted away; and the spasmodic, in which cutaneous itching was followed by numbness and loss of sensation, especially in the extremities, while intermittent spasms weakened the patient and, ultimately involving the respiratory muscles, brought death. Not until the close of the seventeenth century was it discovered that this disease was the result of chronic poisoning caused by the consumption of bread made from blighted rye; the physician of the Duke of Sully demonstrated the presence in spoiled rye of a substance called ergot, subsequently identified as the sclerotium of the fungus Claviceps purpurea. Despite the discovery of its cause, ergotism continued to occur in epidemic form throughout the countries of Europe until the nineteenth century, and sporadic cases are still encountered.

During the same period which saw the identification of ergot as a cause of disease, another phase in its history was beginning—the recognition of its therapeutic uses. The alkaloid ergotine, the active principle in the curved, dark purple grains, is the most powerful known stimulant of the pregnant uterus and has the merit of causing rhythmic contractions. Yet it was long before the value of the drug was recognized by the medical profession. Midwives in Germany and France were using it during the seventeenth and eighteenth centuries; its use in inexperienced hands was apparently attended by fatal errors, for legislation forbidding its employment was passed in several localities. Nevertheless the practice persisted, spreading slowly through Europe and thence to America. In the early nineteenth century "some ignorant Scotch woman, in the county of Washington," New York, was using this powerful agent with such striking results that her work drew the attention of John Stearns, a physician at Waterford in the neighboring county of Saratoga. He took up the clue thus presented, gave long and careful study to the action of ergot, and then, by his publications on the subject, secured professional acceptance of the drug as an obstetric agent.

John Stearns, born in Wilbraham, Massachusetts, in 1770, graduated from Yale College at the age of 19. He then entered upon medical studies under the direction of the distinguished Dr. Erastus Sergeant, of Stockbridge, Massachusetts. In 1792, Stearns went to Philadelphia, where he studied for a year under such prominent teachers as Benjamin Rush, Caspar Wistar, and William Shippen. He then settled in Waterford, New York, and began the practice of his profession.

Stearns's work with ergot began shortly after the turn of the century. On learning of its employment by a Scottish midwife, he procured a supply of the drug from a field of rye and entered upon cautious experiments in its use. These were completely successful, but only after several years of trial did he seek to publish his findings. At length, on January 25, 1807, he wrote a letter on the subject, in response to a request addressed to him by Mr. S. Akerly. This letter, the first step toward the general acceptance of



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in Virginia and Maryland, (for in North-Carolina we have both kinds) that no man will use the latter if he can procure the former for ship or house building, or even for fences. We distinguish this by the name of the *long-leaf*, that by the name of the *short-leaf* pine. We plank all our vessels entirely with this *long-leaf* pine, or, more accurately speaking, that variety of it called the *pitch* pine; with the variety called the yellow pine, we make all our tree-nails, best flooring plank, window-sashes, &c. the grain of the wood being very fine and of a light yellow colour. There are several different species of the short-leaf pine among us, one of which grows in low swampy ground: this is the largest of all our pines, and would be preferable on that account for many purposes, were it not that it is not so durable; the wood of this tree very much resembles in colour that of the long-leaf yellow pine, but is not so fine grained. The *long-leaf* pine with us shoots up in many instances to the height of sixty or seventy feet, is not more than twelve or fifteen inches through, and is very fine for small spars, as it is almost entirely free of knots. If its cultivation could be introduced into the state of New-York, it would, I conceive, be very valuable, particularly for ship building; for it is known by experience, that in the West-Indies and other places where the worm is very destructive to the bottoms of vessels, they will destroy such as are made of oak plank much sooner than those of the pitch-pine." These seeds have been sent to the botanical garden at New-York for experiment.

Account of the Pulvis Parturiens, a Remedy for quickening Child-birth.

In a letter from Dr. John Stearns, of Saratoga county, to Mr. S. Akerly, dated Waterford, January 25, 1807, is the following narration.

"In compliance with your request I herewith transmit you a sample of the *pulvis parturiens*, which I have been in the habit of using for several years, with the most complete success. It expedites lingering parturition, and saves to the accoucheur a considerable portion of time, without producing any bad effects on the patient. The cases in which I have generally found this powder to be useful, are when the pains are lingering, have wholly subsided, or are in any way incompetent to exclude the foetus. Previous to its exhibition it is of the utmost consequence to ascertain the presentation, and whether any preternatural obstruction prevents the delivery; as the violent and almost incessant action which it induces in the uterus precludes the possibility of **turning** . . . In most cases you will be surprised with the suddenness of its operation; it is, therefore, necessary to be completely ready before you give the medicine, as the urgency of the pains will allow you but a short time afterwards . . ."

Fig. 1. The opening page of the first account published by John Stearns on the obstetric use of ergot, as it appeared in the issue of The Medical Repository for November-December, 1807, January, 1808. (From the author's collection)

ergot as an obstetric agent, was published in the *Medical Repository*, 1807-1808 (see fig. 1). It is a brief and temperate document, giving a concise account of the action of ergot and indicating the dangers involved in the use of the drug:

"It expedites lingering parturition, and saves to the accoucheur a considerable portion of time, without producing any bad effects on the patient. The cases in which I have generally found this powder to be useful, are when the pains are lingering, have wholly subsided, or are in any way incompetent to exclude the foetus. Previous to its exhibition it is of the utmost consequence to ascertain the presentation, and whether any preternatural obstruction prevents the delivery; as the violent and almost incessant action which it induces in the uterus precludes the possibility of **turning** . . . In most cases you will be surprised with the suddenness of its operation; it is, therefore, necessary to be completely ready before you give the medicine, as the urgency of the pains will allow you but a short time afterwards . . ."(1)

The publication of this letter brought to Stearns numerous queries from physicians throughout the country, to each of whom he at once sent samples of ergot, with directions for its use. In the course of a few years thereafter, misadventures caused by improper use of ergot occasioned the development of a vehement controversy. Eminent physicians disputed about the value of the drug for over a decade; then Stearns himself, in 1822, placed ergot on a firm footing with the publication of an essay which is a classic in the literature of obstetrics, his "Observations on the Secale Cornutum, or Ergot, with directions for its use in Parturition." In this able work he described completely and in detail his method of using ergot in expediting labor, and specifically defined the indications for the administration of the drug. He pointed out the errors commonly committed in prescribing ergot and the dangers of its use in unpracticed hands, then expressed anew his conviction as to the value of the drug.

Stearns's long championship of ergot greatly augmented his professional reputation and brought him many honors, though his abilities were such as would have brought him to the head of his profession even without this fortuitous discovery. Largely responsible, in 1807, for the formation of the Medical Society of the State of New York, he was elected secretary at the first meeting of the organization and retained this office for several years. From 1809 until 1813 he served in the senate of the state of New York, transferring his practice in 1810 to Albany, where he remained for nine years. He then removed to New York City and for the remainder of his life practiced there, prominent as a consultant and industrious in contributing to medical periodicals. He was for four years the president of the Medical Society of the State of New York, and in 1846 became the first president of the New York Academy of Medicine. In 1848, at the age of 78, he received a dissection wound while performing an autopsy; septicemia developed, resulting in his death.

Stearns's contribution to the cause of obstetrics was one of lasting value. For almost twenty years he labored with singleness of purpose and admirable caution to prove and to impress upon his colleagues the worth of a drug which has saved thousands of lives since his day and which is still in use.

—J. C. T.

1. Stearns, John: Account of the Pulvis Parturiens, a Remedy for quickening Child-birth, in *The Medical Repository*, Second Hexade, 5:308-309, 1807-1808.

North Carolina Medical Journal

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MARCH, 1947

THE HANES MEMORIAL ISSUE

This month's number represents the first memorial issue of the NORTH CAROLINA MEDICAL JOURNAL ever published. It is fitting that this, the first of three consecutive memorial issues, should be dedicated to Dr. Frederic M. Hanes. He was a member of the editorial board of the JOURNAL from its beginning until his death a year ago, and deserves much credit for its success. No one offered more constructive criticism than he, and no one took more pride in its appearance.

The papers presented in this month's issue have all been contributed by members of the Duke medical faculty, who have been associated with Dr. Hanes as students, as house officers, or as colleagues in the Department of Medicine. Dr. Lamar Callaway deserves especial credit for conceiving the idea of a memorial issue, and for supervising the preparation of the articles. It is hard to think of a tribute that would have pleased Dr. Hanes more than this splendid collection of papers, each written as a labor of love, which make up a sort of literary wreath to his memory.

* * * *

THE PLIGHT OF OUR PUBLIC SCHOOLS — A WARNING

An editorial in *New York Medicine* for March 5 is especially timely just now, in view of the plight of the public school system—not only in North Carolina, but in the whole nation. The editorial discusses the argument that has been used for many years by the advocates of compulsory health insurance: "that just as education has been socialized—by requiring every child to attend a public school or its equivalent until he reaches the middle teens—so medical care might well be socialized by public employment of doctors through universal taxation."

The editorial continues:

"Those who argue that the analogy is a sound one must accept the consequences of the analogy. For, if our public education system has its triumphs it also has its failures and its weaknesses. Nearly everyone is aware of the sad plight of the teaching profession as a result of the economic inflation that has taken place in the last year or two. The real wages of school teachers and college instructors, which were never anything to boast about, have in effect been sharply reduced by a soaring cost of living. Moreover, the social position of teachers has been catastrophically depressed in relation to many unskilled occupations through the enormous increases in wages levels that have been forced by trade union action.

"The inevitable result has been that fewer and fewer people are entering the teaching profession, more and more teachers are leaving the profession and the morale of those remaining in the ranks has sunk into the ooze at the bottom of the lake.

"Benjamin Fine, in a series of remarkable articles on conditions in the nation's schools and colleges, appearing recently in the **New York Times**, reports that America's schools today employ 125,000 teachers on emergency or sub-standard licenses. One out of every seven teachers—15% of the total teaching body—cannot meet even the minimum requirements of her state, Mr. Fine revealed, whereas, before the war only 2,300 teachers or one out of every 400 held sub-standard certificates. 'The phenomenal growth in the number of poorly qualified teachers,' says Mr. Fine, 'is the most appalling development in the history of the free public schools.' Eighty thousand of the emergency teachers, he finds, have had less than 2 years of college training and 36,000 have never gone beyond high school. 'As a result of this indiscriminate employment of teachers, the professional standards of the nation have been lowered,' Mr. Fine asserts.

"Mr. Fine quotes a special commission of the National Education Association, which is attempting to raise the professional status of the teachers, as having asked him, 'Would you go out and license 125,000 laymen to practice medicine? Even though we had a shortage of doctors during the war we did not lower the medical standards. Why should we

countenance this in the case of teachers?'

"The picture is disheartening. It should serve both as a warning and a rebuke to any who would urge the dangerous analogy of public medical care as a counterpart of public education. The plight of the teaching profession in our inflating economy would be matched, probably surpassed, by the plight of the medical profession if it were so unfortunate as to be dependent for its economic support upon the public purse. After all, there are nearly a million teachers but only about 150,000 doctors of medicine. Moreover, teachers are at least to some degree unionized and they serve in large groups under local authorities. Teachers can strike against intolerable conditions, and in so doing they often gain considerable public support for their demands. Doctors could not conceivably operate in comparably large units, they have an inherent repugnance for labor union tactics and any strike against the public by doctors of medicine, however well justified, would destroy forever their professional prestige, for a medical strike would directly threaten the very lives of the citizens. If, therefore, the teachers find it difficult to wrest even a modicum of economic justice out of the lethargic public and their timorous political servants, what hope would there be for a politically impotent medical profession in a similar situation?

"It is possible to build up a formidable case for the proposition that our public system of education has, by and large, failed in its primary function—that of producing educated, integrated and balanced adult human beings. But that is another story. The drastic deterioration of the teaching profession, which we are witnessing today—and the alarming lack of concern regarding this situation amongst most people—should be more than ample warning against any who would trot out this lame old analogy once again."

* * * *

DR. H. S. WILLIS HEADS STATE TUBERCULOSIS SANATORIA

On February 27 the Board of Directors of the North Carolina Tuberculosis Sanatoria elected Dr. Henry Stuart Willis as superintendent of the three state institutions, to succeed the late Dr. Paul McCain. Dr. Willis is now medical director and superintendent of the Detroit Municipal Tuberculosis Hospital (the William H. Maybury Sanatorium) at Northville, Michigan, and is well known throughout the nation as a clinician and as an administrator. In coming to North Carolina, Dr. Willis is really coming back home. He was born in High Point and was graduated from the University of North Carolina before getting his medical degree from Johns Hopkins in 1919.

An excerpt from a personal letter written by a member of the house staff of the Maybury Sanatorium offers the best possible recommendation of Dr. Willis. It means all the more because the writer had no idea that any part of the letter would be quoted.

"North Carolina is indeed fortunate to get Dr. Willis to go to head the State Sanatoria. How we do hate to lose him! But it will be a good thing for North Carolina. I was much surprised at his decision to go there; I had not felt that the state could get such a good man to follow Dr. McCain, who was one of his very good friends."

As Dr. Willis assumes his duties on April 15, he may be sure of a warm welcome "back home" from the doctors of North Carolina. They know that the mantle of his friend, Paul McCain, has fallen on worthy shoulders.

* * * *

THE C. M. A. B.

C. M. A. B. is not another alphabetical agency of the government, but is the abbreviation for the Cooperative Medical Advertising Bureau of the American Medical Association. This agency performs a most important function in securing advertisements for most of the state medical journals published in the United States. The fact that medical preparations accepted by this bureau must meet the requirements of the Council on Pharmacy and Chemistry means that they are dependable.

The C.M.A.B. is strictly a non-profit organization, and the efficiency with which it is managed is proved by the fact that the accounts which it handled for its constituent state journals in 1946 amounted to more than $600,000, and that the total expenses of the bureau will be less than 5 per cent of this amount.

The NORTH CAROLINA MEDICAL JOURNAL has had its full share of this advertising, and to the firms which advertise in the pages of the JOURNAL are due thanks for making its publication possible. Our subscribers can best express their thanks by patronizing these firms, and can help to increase the volume of advertising by saying that they saw the product advertised in the NORTH CAROLINA MEDICAL JOURNAL.

* * * *

WAXHAW NEEDS A DOCTOR

In this month's issue will be found an advertisement which may be of interest to some young doctor just out of service, who wants to begin work at once as a general practitioner. The town of Waxhaw, in Union County, is without a doctor, and the people who live there and in the surrounding territory are in need of someone to whom they can look for medical care. Mr. Robert Howie writes that the hospital in Monroe, 12 miles distant, would be available to a doctor located in Waxhaw. Anyone interested may communicate with Mr. Howie.

MEDICOLEGAL ABSTRACT

J. F. OWEN, M.D., LL.B.
RALEIGH

WILLS: *Oral disposition of personal property is legal under certain circumstances.*

This case revolves about the legality of a nuncupative will—a type of will which is little known and which, although oral, meets the legal requirements for bequeathing personal property and this type of property only.

The records show that a man suffering from the last stages of tuberculosis, and having neither time nor strength to make use of a written will, directed orally that his bank draw a cashier's check for the full amount of his account, payable to his sister at his death. Shortly after making this request the donor died, and the bank, following directions, paid the money to the person named.

The executor of the decedent's estate promptly filed suit in circuit court for the purpose of securing possession of the property covered by the nuncupative will. The lower court rendered judgment in favor of the bank and the sister, who had entered the case as a co-defendant. The executor, in behalf of the estate, appealed to the Supreme Court, alleging failure of delivery of the property as required by law in such cases. The appellate court stated that a gift *enter vivos* must be fully consummated and vests ownership in the donee beyond the power of the donor to recall. In the case of a gift *causa mortis* absolute title does not immediately take effect, and is subject to the will of the giver; in the event of death the title passes to the donee, but until that time the donor has the power to dispose of the property as he wishes. The court in this case ruled that there was sufficient delivery, the gift being in the hands of a third party, the bank. The judgment therefore was in favor of the bank and the beneficiary.

In general a testator in good health and having sufficient time at his disposal would naturally arrange for his bounty after death by utilizing either the written, attested will or the holographic will, the latter being a will written in the handwriting of the donor, requiring no witnesses, and deposited among his valuable papers for reference at the proper time. The nuncupative will, such as the one involved in the case discussed above, is applicable only to personal property and is resorted to by sick persons in anticipation of death. This type of will is legal in the State of North Carolina, but in order to prevent fraud is surrounded by numerous legal requirements as to the act of disposition and also as to probation. Briefly, the person desiring to make an oral will is required to secure two competent persons who must be charged by him to "bear witness" to the transaction, and his wishes must be reduced to writing for the purpose of probation within ten days.

Inasmuch as physicians are frequently in a position to help in such matters, a knowledge of the fundamentals of testamentary disposition of property is desirable. In emergencies due to illness, where neither time nor the testator's condition is such as to enable him to write or dictate his wishes, the attending physician may be called on to "bear witness" to a nuncupative will. (Supreme Court of Michigan, V. 295 N.W. Reporter, p. 266, December, 1940.)

TUBERCULOSIS ABSTRACTS

A Review for Physicians

Issued Monthly by the National Tuberculosis Association

Vol. XX **March, 1947** **No. 3**

MANY family physicians with long experience have entertained more than a mere suspicion that individuals belonging to certain families show relatively little resistance to infection with the tubercle bacillus. Now statistical evidence to support such an observation has begun to accumulate. This is of practical importance to both physicians and health officers since a case of tuberculosis in such a family calls for an intensification of all protective measures if spread of the disease within that family is to be prevented.

SPREAD OF TUBERCULOSIS IN FAMILIES OF TUBERCULOUS PATIENTS

A tabulation of the family records of patients with active tuberculosis under the supervision of the Los Angeles County Health Department has uncovered some surprising facts regarding the susceptibility of the members of certain families to the spread of this disease.

The figures show that nearly all of the new cases originate in a comparatively small proportion of the families exposed. These susceptible families deserve earnest study. Preventive measures within them can be successful only as they are directed toward the major elements of spread. What these elements are is still unknown. A family is a complex unit, exhibiting characteristics, traits, and habits that have been in operation for generations. Even

though the faults of these families may not be easily corrected, if they can be defined so as to be recognized, they can be made the object of intensive health supervision. If tuberculosis is to be prevented among them, these families must have larger proortions of the tuberculosis prevention budget than is ordinarily allotted to them.

It is characteristic of tuberculosis in Southern California that it is concentrated in a few comparatively congested areas, inhabited chiefly by families in the low income brackets. Here many conditions favor the spread of disease. In planning surveys and applying special preventive measures, tuberculosis attack rates must be given careful consideration. Local surveys in Los Angeles with a house-to-house canvass in poor neighborhoods have detected five times as much active pulmonary tuberculosis as has been found by the same amount of effort expended in other types of surveys. More information about the reasons for spread in the homes where tuberculosis thrives is urgently needed. In these homes, the wage-earner, all other adults and the older children must be examined.

Crowded living quarters constitute a major fault. In spite of improvement, economic conditions must still be considered a factor. Although thousands of these families have moved to modern housing projects and many have been earning big wages, too often they have reverted to old living habits within the new dwellings. These habits have been gradually molded into characteristics that will require long and painstaking efforts to change.

In 1940, the Los Angeles County Health Department analyzed the family records of all the cases of active reinfection type tuberculosis. All cases found in the family within six months of the time that the first case in the family was diagnosed in the clinic were regarded as original cases. Only those detected thereafter were considered new cases whose infection was presumably due to exposure during the period of observation. Contacts with no active tuberculosis were not included in the tabulations unless they had been under observation six months or longer.

There were 506 families with 595 original cases and 1,637 other persons exposed. There were 135 new active cases developing among these exposed persons, or 8.25 per cent. Of these, four were active nonpulmonary, 45 were active primary and 86 active reinfection type pulmonary tuberculosis. In other words, slightly more than five per cent of the 1,637 contacts developed active reinfection type pulmonary tuberculosis six months or more after the discovery of the first known case in each of the respective families.

These data cover experience during the latter half of the 1931-1940 decade, during the worst years of the depression. Now, four years later, the present active cases have been analyzed, eliminating the families previously tabulated. Unquestionably, there was improvement in the economic status of these families. There was less cause for congestion within the home, and with better living conditions and improved nutrition there should have been less likelihood of the spread of infection. The average number of months of exposure of contacts was also less, because of improvement and extension of the isolation technique. In spite of all this the results show that the justifiable prediction of a lower attack rate would be in error. In 431 families with 1,264 contacts, 60 cases of active reinfection type pulmonary tuberculosis developed among the contacts, or an attack rate of 4.75 per cent. This is very little lower than the rate found in the previous survey.

The hazard in these families with this high attack rate is apparently not only due to the direct spread of the infection, but to other conditions favoring the spread. There must be some inherent fault either in their physical or their mental make-up which makes the members of these families more susceptible than the average person; or there may be contributory domestic habits unchanged by the usual public health education and supervision.

Conditions in other families in similar communities were found to be quite different. The X-ray surveys previously mentioned were carried on in the most congested parts of these same areas, and 22,000 persons examined showed an attack rate of 0.5 per cent. The greater tendency to spread in certain families, in comparison with other families, is demonstrated by the fact that in families having more than one case, even where no positive sputum can be found, there is a high attack rate.

With this high attack rate in certain families, it would seem justifiable to isolate outside of the home every active case occurring in a family with a history of considerable tuberculosis. The effectiveness of such a ruling was shown in a small neighborhood where nine deaths occurred in eighteen months. An arbitrary edict was issued that no active case would be permitted to remain at home in that neighborhood. This stopped the spread and there have been no new cases. In another district, where there were a number of ex-sanatorium, chronic, advanced, communicable cases it was found possible to isolate within the homes with extra assistance. This procedure was found to be effective in stopping the spread of infection. In this type of family isolation is essential. The cases found should not be permitted to remain at home unless considerable material assistance is available and intensive supervision is supplied.

Spread of Tuberculosis in Families of Tuberculous Patients, P. K. Telford, M.D. and Ruth Garten-White, M.D., American Review of Tuberculosis, March, 1946.

CORRESPONDENCE

VETERANS ADMINISTRATION
310 W. Fourth Street
Winston-Salem, N. C.
March 7, 1947

To the editor:

The Veterans Administration has established a goal of "Medical Service Second to None" in order to insure that veterans who served this country in time of war receive proper medical attention. The attainment of this goal in North Carolina, as well as elsewhere, will be extremely difficult unless qualified physicians associate themselves with this program.

I am hoping that we will be able to reach interested doctors through the pages of the NORTH CAROLINA MEDICAL JOURNAL. There exists immediate need for physicians in our out-patient clinics at Winston-Salem, Charlotte and Durham, North Carolina. Doctors in these cities will be considered for full time or part time association with the Veterans Administration.

An adequate salary with periodic pay increases, numerous professional advantages and other factors, we feel, will interest physicians who heretofore lacked information about the Medical Program of the Veterans Administration. Full details may be obtained from the Manager of the Veterans Administration, Sub-Regional Offices in Charlotte and Durham or from the Personnel Officer, Veterans Administration, Regional Office, Winston-Salem, North Carolina. I will be glad to answer any inquiries from physicians in this regard.

North Carolina has more than 340,000 veterans of World War II and over 70,000 veterans of other wars. In the interest of those who require medical attention or treatment, I am making this appeal to doctors to associate themselves in our program.

Very sincerely yours,

A. J. WEIRICK, M.D.
Chief Medical Officer

* * * *

THE STATE SOCIETY MEETING

March 7, 1947

Dr. Robert M. Fales, President
New Hanover County Medical Society
Wilmington, North Carolina

Dear Dr. Fales:

I enclose the card sent out by the New Hanover County Society. It may not be returned without comment.

Had your Society offered the State Association 500 beds at Wrightsville for the annual meeting, that would have been valuable constructive criticism. As it is you offer nothing except destructive criticism and ignore the tremendous expenditure of thought, time, planning and effort on the part of our State Medical Society Executive Committee. Furthermore, the question is so worded that the results might easily be interpreted in any way desired.

There is sufficient strife, bitterness, wrangling and contentiousness in the land already without deliberately seeking to add more. Let's leave that sort of thing to the textile unions and the United Mine Workers.

To a casual observer this looks like an effort on the part of a small group of doctors to discredit the duly elected and hard working officers of the State Medical Society. It might seem that the New Hanover County Society might more gracefully either secure adequate accommodations for the meeting at their own beach or remain away from the Virginia Beach meeting in dignified silence.

Very truly yours,

S. F. RAVENEL, M.D.
JEAN MCALISTER, M.D.

CC: NORTH CAROLINA MEDICAL JOURNAL,
Winston-Salem, N. C.

BULLETIN BOARD

PRESIDENT'S MESSAGE

DINOSAURS

It is the custom of Dr. Kelsey Regen, the able and beloved minister of the First Presbyterian Church in Durham, to present a five-minute sermon for the children at each Sunday morning service. A few Sundays ago he announced to the children that he wished to speak to them about dinosaurs. Without attempting to quote him, I wish to try to reconstruct his little sermon as I recall it, placing some emphasis upon the points he made as I remember them.

Said Dr. Regen, "I wish this morning to speak to you children about dinosaurs. How many of you have seen pictures of dinosaurs?" Every child had. "You know that many, many years ago there were thousands upon thousands of dinosaurs roaming all over the earth. They were large, powerful beasts. But somehow they disappeared. Today there is not a single dinosaur in the whole, whole world. Can anyone tell me why they disappeared, why there is none today?"

A smart little boy answered, "Their bellies were too big and their heads were too little." Said the kindly minister, "That may be true, but I hardly think that is why they disappeared. In all these pictures of dinosaurs that you have seen, what are they always doing?" A smart little girl said, "Fightin'." "That is right," said the good preacher, "and that is where we may find the cause of their disappearance."

He continued, "It seems that dinosaurs did not get along very well together. They always had arguments. One dinosaur never was willing to help another. Every one had his own ideas and was ready to fight every one who did not have the same views. It was always one against the others. They were probably not all bad, but they just could never get together and work as a team. Maybe they were not all opposed to each other; but each likely had some 'reservation,' how-

ever slight, that kept him from quite going along with those around him. This led to arguments.

"Then too, the other beasts of the day soon learned that the dinosaurs were not united. They did not respect them and found them easy prey. If they attacked a dinosaur they could defeat him because one dinosaur seldom helped another.

"And so it went on, ages upon ages, and the dinosaurs gradually lost ground. They had no unity of purpose. It was every dinosaur for himself. It never dawned upon them that they might unite and help each other. As a result of all of this, they just simply disappeared—ceased to exist, because they couldn't get along together."

And then the good preacher said, "You children know that for years and years and years, we have had bees and ants, and today there are very many of them. They seem to be doing fine. Do you know why they are doing so well; why they are leading such happy lives?"

Each little hand went up, because every little child knew the answer.

* * * *

FREDERIC MOIR HANES

The dedication of this issue of our JOURNAL to the memory of Dr. Fred Hanes will meet with widespread approval of the membership of the Society. The editorial board is to be congratulated.

Duke University and the State of North Carolina suffered a great loss in the passing of Dr. Hanes on March twenty-fifth of last year. A native North Carolinian, he rendered valuable service to his state as a physician and teacher of medicine. His scientific attainments resulted in many honors' being conferred upon him, not only in his native state but throughout the nation.

It was not my privilege to have many close professional contacts with Dr. Hanes, but his colleagues knew him as a keen clinician and an able teacher. He inspired his students to a high type of scientific endeavor. His work will remain a tradition in the Duke Medical School that will stimulate his associates and students for many years to come.

Socially, he was a cultured gentleman who was most considerate of those about him. On the golf course, he was an earnest golfer who loved the game, companionable and pleasant; it was always a pleasure to play with him. In this sphere I knew him best and I shall always cherish the association of the games we had together.

Dr. Hanes had a breadth of vision and loyalties that marked him as a truly great man. He was interested in all things that made for better medicine and its wider distribution to the masses of the people. He made contributions to Duke University and to the state that must be perpetuated. His life and work will, for years to come, set an example for accomplishment that many will strive, with credit, to equal, but few will attain.

W. M. COPPRIDGE, M.D.

STATE BOARD OF MEDICAL EXAMINERS

The next meeting of the Board of Medical Examiners of the State of North Carolina for the purpose of licensure by endorsement of credentials will be held on Thursday, May 1, 1947, at the Sir Walter Hotel in Raleigh. The meeting set for April 30 in Winston-Salem has been cancelled.

* * * *

An extra session of the North Carolina State Board of Medical Examiners was held at the Sir Walter Hotel in Raleigh, January 15, 16, and 17, 1947. Sixty-three physicians were licensed by endorsement of credentials. Seven physicians were declined license because of failure to meet the requirements of the board or failure to graduate from a class A medical school. Two of these were foreign graduates.

Dr. M. was called before the board on account of repeated narcotic violations and other offenses. The license of this physician had been revoked by a former board. The physician claimed reinstatement but was advised of his error and warned not to practice medicine. Councilor Donald B. Koonce of Wilmington assisted the board in the hearing of this case.

The case of Dr. A., who had been convicted in Haywood County on the charges of fornication and adultery and maintaining a building for prostitution and assignation, was heard. The physician's three attorneys presented eleven witnesses who testified generally that the physician was in good standing except for the single Haywood County affair. There were no prosecuting witnesses, only the evidence of admission and conviction in the court record. After due deliberation and consideration of all the facts, the board ordered the license of Dr. A. to be revoked and rescinded; this order was suspended, however, upon condition that Dr. A. "be and remain of good behavior; that he not violate any criminal law; that he be of good moral conduct, and that he practice medicine on a high professional plane and in an ethical manner for a period of five years from this date."

The following resolution was passed and forwarded to the Medical Care Commission:

"BE IT RESOLVED: That the State Board of Medical Examiners endorses the entire plan as recommended by the Medical Care Commission. The board realizes that the Medical Care Commission has made a thorough study and outlined a competent program based upon the great need for additional facilities and medical personnel in North Carolina. The State Board of Medical Examiners realizes the fact that an adequate number of physicians have not been obtained by the sources available within and outside of the state."

The North Carolina League for Crippled Children

Every year the North Carolina League for Crippled Children joins in the national sale of Easter seals, proceeds of which are used in a continuous program to advance the welfare of crippled children and adults. This year the sale is being put on from March 6 to April 6.

The North Carolina League for Crippled Children is a private charitable organization that cooperates with but does not duplicate the work of other public or private agencies. It aids the crippled throughout its area of all ages, races, and creeds, whether crippled through birth, disease or accident. Its only condition for aid is a valid need not otherwise provided for. Its only source of funds is voluntary contributions received from the annual sale of Easter Seals.

The sale of Easter seals offers an opportunity for all citizens to share in this important work of building crippled children into happy and useful men and women. If you have not received seals in the mail and wish to contribute, write the North Carolina League for Crippled Children, Box 839, Chapel Hill, N. C.

News Notes from the North Carolina Tuberculosis Association

Available from the state office is a well illustrated pamphlet entitled "Surgery in Tuberculosis" prepared by Dr. R. H. Overholt and Dr. N. J. Wilson. It discusses the following surgical procedures: phrenic nerve paralysis, pneumothorax, pneumonolysis, thoracoplasty, lobectomy, pneumonectomy, pneumoperitoneum, extrapleural pneumothorax and cavity drainage. The price is $8.00 a hundred or 10¢ each in units of less than one hundred.

News Notes from the Duke University School of Medicine

The Duke Medical Alumni will hold their second reunion on April 24, 25, and 26. The following program will be presented by Duke graduates and men who trained at Duke.

Thursday morning, April 24
- Registration

Thursday afternoon
- Dr. O. J. Bateman ('39)—"Use of B.A.L. in Gold Poisoning"
- Dr. Charles Styron ('38)—"The Genito-Urinary System in Diabetes Mellitus"
- Dr. George Harrell ('36)—"Plasma Volume and Extravascular Thiocyanate Space in Rickettsial Spotted Fever"
- Dr. B. B. Dalton ('32)—"Meeting the Problems of the General Practitioner"
- Dr. P. B. Parsons ('36)—"Intra-Abdominal Herniation: Its Radiological Diagnosis"
- Mock Clinic (by junior and senior students)
- Class and/or Departmental entertainment

Friday, April 25
- Dr. George Gilbert (house officer, 1939-44)—"The Cellular Changes in Carcinoma of the Prostate Following Hormonal Therapy"
- Dr. Paul Reque ('34)—"An Evaluation of the Use of Antibiotics in Dermatology"
- Dr. J. S. Hiatt, Jr. ('40)—"Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis"
- Dr. David Wilson (house officer, 1942-46)—"Lucite Balls in the Treatment of Pulmonary Tuberculosis"
- Dr. Harold H. Kuhn ('40)—"Open Versus Closed Treatment of Acute Osteomyelitis"
- Exhibits
- Business Meeting
- Presentation of New Officers
- Reunion of 65th General Hospital and 38th Evacuation Hospital—
- Open House—Local Alumni
- Dinner-Dance—Hope Valley Country Club

Saturday, April 26
- Dr. Eleanor Easley ('34)—"A Study of Maternal Morbidity with the Use of Caudal Anesthesia"
- Dr. Robert H. Pudenz ('35)—"Cranial Trauma and Brain Movement. Direct Observation of the Brain with High Speed Cinematography"
- Dr. R. H. Rigdon (house officer, 1931-35)—"Consideration of the Mechanisms by which a Rapid Diminution Occurs in the Parasitemia in Ducks Infected with P. Lophurae"
- Dr. David A. Young (house officer, 1935)—Title later
- Dr. Charles W. Hock ('41)—"Radiation Injuries of the Intestines"
- Duke-Navy Baseball game

* * * *

Dr. James G. Whildin was appointed to the staff as associate in radiology on January 21, 1946, after spending five years in the army.

* * * *

The Technical Division of the Department of Radiology, under the supervision of J. B. Cahoon, Jr., R.T., has increased lectures and demonstrations in order to offer postgraduate instruction to outside technicians who need refresher courses. Two students are admitted for the accredited course in x-ray technical training each March and October. A nursing degree, college diploma, or former technical training is a prerequisite.

* * * *

Miss Helen Kaiser, director of physical therapy, has recently returned from Greece, where she was active in the Near East Foundation. The Foundation has established a Physical Therapy School, which has been set up by experienced American personnel. Adequate supervision will be given to the students during their training and first years of work experience. The course has been set up to meet the requirements of the American Medical Association, and upon completion of their present course of twelve months two students will be selected for further study in physical therapy at Duke University.

* * * *

Dr. Watt W. Eagle addressed the Southern Section of the American Laryngological, Rhinological and Otological Society on January 6 at Miami Beach. His topic was "Elongated Styloid Process—Further Observations and a New Syndrome."

News Notes from the Bowman Gray School of Medicine of Wake Forest College

The Board of Trustees of the North Carolina Baptist Hospital and the Board of Trustees of Wake Forest College met on March 11, 1947, and adopted the following resolutions:

"1. That this group here assembled recommends that the hospital and medical school be relocated on Graylyn Estate adjacent to the new Wake Forest College campus; and

"2. That a general campaign be launched immediately for the purpose of raising $6,000,000 from individuals, foundations and other sources to provide

funds for a complete plant in the new location; and

"3. That the campaign for funds be a joint effort with Wake Forest College in connection with raising funds to move Wake Forest College to Winston-Salem."

* * * *

Dr. C. C. Carpenter, dean, recently announced the appointment of Dr. Henry Shepard Fuller of Washington, D. C., as assistant professor of preventive medicine. Dr. Fuller will assume his duties on October 1. Dr. Fuller is at present taking a course at the London School of Hygiene and Tropical Medicine, as recipient of the Moseley Traveling Fellowship from Harvard University for 1946, which entitles him to a year's study in Europe.

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Dr. Franklin Henley has been appointed to the staff as instructor in clinical pediatrics. He is a graduate of Davidson College, the Medical School of the University of North Carolina, and Harvard University School of Medicine.

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Dr. W. C. Thomas of the Department of Pathology has been granted a year's leave of absence, effective July 1, 1947, for further study in one of the country's leading universities.

Fourth District Medical Society

The Fourth District Medical Society met in Goldsboro on February 14. Dr. Reno Porter of Richmond, Virginia, was guest speaker. Officers of the Society are Dr. Claiborne T. Smith of Rocky Mount, president; Dr. Herman F. Easom of Wilson, vice president; and Dr. Robert M. Whitley of Rocky Mount, secretary-treasurer.

Catawba Valley Medical Society

The Catawba Valley Medical Society held its regular meeting in Lenoir on February 18. Speakers on the program were Dr. Charles M. Kendrick, Dr. Shelton Fowler, Dr. Ralph E. Lore, and Dr. Frederick M. Dula, all of Lenoir. A film on sulfathalidine in the treatment of ulcerative colitis was also presented.

Edgecombe-Nash Counties Medical Society

The regular monthly meeting of the Edgecombe-Nash Counties Medical Society was held in Rocky Mount on February 12. Dr. C. W. Bailey presented a paper on "Problems of Deafness in Children," and Drs. C. T. Smith and W. S. Wall discussed the question of whether or not a colored hospital is needed in Rocky Mount.

Forsyth County Medical Society

Dr. Leland S. McKittrick, associate professor of surgery at Harvard Medical School, was guest speaker at the meeting of the Forsyth County Medical Society held in Winston-Salem on February 11. His subject was "The Diagnosis and Treatment of Surgical Conditions of the Biliary Tract."

Halifax County Medical Society

The Halifax County Medical Society held its regular monthly meeting in Roanoke Rapids on February 14. Dr. Paul Douglas Camp of Richmond, Virginia, discussed the "Differential Diagnosis of Rheumatic Fever and Syphilitic Heart Disease."

News Notes

Dr. Henry Stuart Willis, superintendent of the William H. Maybury Sanatorium in Northville, Michigan, has been selected to succeed the late Dr. Paul P. McCain as superintendent of the three state tuberculosis sanatoria. Dr. Willis was born near High Point, North Carolina, and is a graduate of the University of North Carolina and Johns Hopkins Medical School. He has been associated with the Maybury Sanatorium for the past seventeen years. He will assume his new duties on April 15.

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Drs. I. M. Procter and Kenneth Dickinson of Raleigh have announced the association of Dr. Guy Hewitt Branaman in the practice of obstetrics and gynecology.

* * * *

Dr. Millard Jones of Red Oak has recently become associated with Dr. W. S. Wall of Rocky Mount.

* * * *

Dr. Jane Gregory Marrow has opened offices for the practice of obstetrics and gynecology in Rocky Mount.

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Dr. W. K. McDowell of Tarboro has announced the limitation of his practice to diseases of the ear, nose, and throat.

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Dr. George H. Wadsworth is chief surgeon of the new Roanoke-Chowan Hospital in Ahoskie.

* * * *

Drs. Robert A. White and Harmon J. Bailey of Asheville have announced the opening of their new offices for the practice of obstetrics and gynecology.

Sectional Meeting of the American College of Surgeons

Drs. Keith S. Grimson and Deryl Hart of the Duke University School of Medicine appeared on the program of the sectional meeting of the American College of Surgeons, held in Baltimore, March 10 and 11. Dr. Grimson spoke on "Limitations of Transthoracic Vagotomy for Peptic Ulcer," and Dr. Hart presided over a panel discussion on "Postoperative Care."

Army Medical Library Microfilm Service

During the war, the army medical library through its photoduplication services supplied millions of pages of microfilmed medical articles to the armed services and other research agencies.

This service is now generally available for civilian physicians, institutions and research workers on a cost basis. This means direct access to the library's enormous resources of medical literature.

A fee of fifty cents is charged for filming any periodical article in a single volume, regardless of length. Microfilming from monographs is furnished at fifty cents for fifty pages or fraction thereof. Photostats are also available at a charge of fifty cents per ten pages or fraction thereof.

For convenience and to keep bookkeeping costs down, a coupon system has been established. Users may buy any quantity of photoduplication coupons at fifty cents each. Order blanks are available upon request. Checks should be made payable to the Treasurer of the United States, and sent to the Army Medical Library, Seventh Street and Independence Ave., S.W., Washington 25, D. C.

(BULLETIN BOARD CONTINUED ON PAGE 189)

AUXILIARY

ORGANIZATION

A Challenge to Doctors' Wives

The work of the Auxiliary, which is under the guidance of the State Medical Society and the American Medical Association, has materially increased in the past few years; and in order to be of greater assistance to the medical profession in North Carolina we need to enlarge our organization. We need the added strength and influence of an auxiliary in every county that has a medical society.

First, let us review briefly the history of the Auxiliary, its present status, and its future possibilities of growth. This review, perhaps, will give an overall picture of "why" the Auxiliary was formed and will justify its existence.

Someone has said, "No organization can be greater than the cause which brings it into existence, and no group springs suddenly into usefulness but is the gradual outgrowth of ideas that have lived because of their worth."

The Auxiliary to the Medical Society of the State of North Carolina will soon celebrate its twenty-fourth anniversary, having been organized April 18, 1923, in Asheville, with Mrs. P. P. McCain as organizing chairman and first president. There were 53 charter members.

The primary object of the Auxiliary at the beginning was purely social, but as time passed the feeling grew that the demand for a broader vision, greater incentive, and keener endeavor was a challenge to an organization of intelligent women. So as the years have passed, the Auxiliary has grown, not only in membership but in its scope of work, which today embraces social, educational, and philanthropic activities.

It has long been our ambition to reach a membership of 1000. Last year we missed this goal by less than 50. Certainly we should "go over the top" this year.

We now have 28 organized counties; 7 of these were organized last year (5 in the Fifth District), and 1 was reactivated. While this increase is most gratifying, there are still many unorganized counties with active medical societies which would welcome an auxiliary. In the one hundred counties of the state, there are sixty-eight component medical societies or units, representing eighty-one counties. (In some instances two or three small counties are combined; an auxiliary would follow the same pattern.) So we have vast opportunity to expand, and there is an urgent need to do so if we are to go steadily forward.

These, briefly, are the ways in which *you* can help:

Join your local auxiliary.

If your county does not have an auxiliary, help to organize one—today!

If this is impossible, become a member-at-large by sending your dues of $1.00 to the treasurer, Mrs. E. C. Judd, 2108 Woodland Avenue, Raleigh.

We support an organization only when we belong to it and are interested in its objectives and tasks.

Perhaps you have used the argument that women throughout the United States are over-organized, and you have no time for anything more. While it is true that as a doctor's wife you are a busy person and have cares and responsibilities that the average layman's wife does not have, yet what other group—study, civic, or social—should rate priority over your husband's chosen profession?

Through an organization you keep in touch with national, state, and local activities, getting a clearer perspective of its tasks and accomplishments. An organized unit is a medium through which work can be planned and reported.

An Auxiliary member has many opportunities to extend and interpret the aims of the medical profession to other organizations. Today it is very important to direct public thinking and actions in channels approved by the medical profession.

It is manifest that Auxiliary members have experienced much pleasure in the part they have played in keeping guests in the three sanatoria beds and in supporting the Student Loan Fund, not to mention the pleasure derived from social contacts and from becoming better acquainted. These are only a few of the advantages of being an Auxiliary member. The Auxiliary needs *you*; you need the Auxiliary.

Let's try to make this a banner year in organization. To do so, we need the cooperation of every doctor's wife in North Carolina. The accomplishments of the past, the objectives of the Auxiliary, and the mani-

fold opportunities before us are a challenge not only to keep intact the precedents set by our predecessors but to forge ahead to do bigger and better things.

"Let us not be weary in well doing."

MRS. ERICK BELL,
Chairman of Organization
Wilson

* * * *

Haddon Hall will be the headquarters for the Annual Meeting of the Woman's Auxiliary to the American Medical Association, which will be held in Atlantic City, New Jersey, June 9-13, 1947.

Requests for reservations should be sent immediately to Dr. Robert A. Bradley, Chairman, Subcommittee on Hotels, 16 Central Pier, Atlantic City, New Jersey.

BOOK REVIEWS

The Compleat Pediatrician. By W. C. Davison, Professor of Pediatrics, Duke University School of Medicine; formerly acting Pediatrician in Charge, The Johns Hopkins Hospital. Ed. 5. Price, $3.75. Durham, N. C.: Duke University Press, 1946.

It is difficult to conceive of a text which could contain more useful and readily accessible information than the new fifth edition of **The Compleat Pediatrician.** The book is completely cross-indexed, so that differential diagnosis from symptoms is allowed and the salient points of each disease and up-to-date therapeutic measures are provided. There are also sections on general supportive treatment and nursing care containing a wealth of practical information derived from the author's wide experience and careful observations in pediatric practice.

The chapters on laboratory and analytic procedures are comprehensive and yet precise. The sections on nutritional requirements, feeding, and diet include schedules and recipes, not only for the normal pediatric patient but for those having nutritional and metabolic disturbances. Much of the information is presented in easy-to-utilize, tabular form. A list of the drugs and prescriptions most frequently used in pediatrics completes the text.

This small volume is unique in presenting so simply the essentials of pediatrics. It cannot help but enjoy the enthusiastic reception accorded the earlier editions. It is unreservedly recommended to all students and practitioners of medicine, and is a **must** for pediatricians.

Their Mothers' Sons. By Edward A. Strecker, M.D. 220 pages. Price, $2.75. Philadelphia and New York: J. B. Lippincott Co., 1946.

This is the most forceful, hard hitting, "straight from the shoulder" book published in a long time. If it enjoys the popularity which it deserves it could easily be one of the important books of the present generation in America.

Dr. Strecker has analyzed the revered American "mom" and has uncovered, in a very logical manner, the fact that she is not really a very lovable or admirable character. He carefully distinguishes the real mother from the mom, the latter being a "woman who has failed in the elementary mother function of weaning her offspring emotionally as well as physically." He characterizes her as one who "derives [her emotional satisfaction] from keeping her children paddling about in a kind of psychological amniotic fluid rather than letting them swim away with the bold decisive strokes of maturity from the emotional maternal womb," and finally indicts her for her "failure to prepare the child to meet even the minimal demands of adult life."

The importance of this problem is emphasized by the fact that 500,000 men attempted to evade the draft, almost 2,000,000 were rejected for psychiatric disorders, and 600,000 were discharged for neuropsychiatric reasons. Most physicians who had experience with Selective Service either in the army or as civilians will agree that poor training and mental habits inculcated by their parents were responsible for the deplorable mental state of these men.

The author gives a body blow to progressive education in its worst form, calling attention to the obvious, but often overlooked fact that "the only time the 'musts' and 'must nots' of the world . . . can be learned is during childhood."

Occasionally one comes across paragraphs which seem to have been written for physicians as parents. With many busy physicians' children being reared almost exclusively by their mothers, this book deserves the careful attention of every doctor with children. The author shows how easy it is for a wife who is rearing a family with little help from her husband to fall into the ways of "momism" in spite of excellent intentions and education.

Dr. Strecker is a rare character among medical authors. He has something to say and he knows how to say it. This book is not only enlightening but very readable. It is recommended **summa cum laude** to physicians, parents, and all people who have any dealings with children.

Uterine Contractility in Pregnancy. A Study of the Contractions of Pregnancy and Labor Under Normal and Experimental Conditions. By Douglas P. Murphy, M.D., F.A.C.S., Assistant Professor of Obstetrics and Gynecology and Research Associate in the Gynecean Hospital Institute of Gynecologic Research, University of Pennsylvania. 130 pages, with 64 illustrations. Price, $5.00. Philadelphia: J. B. Lippincott Company, 1947.

This volume represents a collection of the numerous studies which have been carried out by Dr. Murphy with the Lorand tocograph. It represents an analysis of more than 3,200 individual records of uterine contraction taken during pregnancy and labor, augmented by studies of those drugs most commonly employed in an obstetric practice. The material contained in the book represents much of clinical value when it is applied to the management

of obstetric problems.

Abnormal deficiency of uterine contractions, with prolongation of labor in the absence of a mechanical obstruction, is present in approximately one patient in twenty-five. It often leads to undue difficulties when the problem is not recognized early in labor and the labor treated accordingly. Murphy points out that this group of patients can be recognized clinically by variation in the type of uterine contraction from the very beginning of labor.

The material in this excellently prepared and arranged monograph is of extensive clinical value for the practical management of obstetric patients, and the book is an excellent academic publication for the student of obstetrics.

All but Me and Thee. By Brig. Gen. E. D. Cooke. 215 pages. Price, $2.75. Washington: Infantry Journal Press, 1946.

The author of this book was ordered by General Marshall to investigate completely the problem of psychoneurosis in the army of World War II. When General Cooke gave his final report, the unique Chief of Staff said to him, "When the necessity no longer exists for keeping these matters confidential, you owe it to our people to share your knowledge with them." This book is the result.

General Cooke interviewed everyone concerned with the problem, from the foxholes all the way to Washington. The subtitle of the book, "Psychiatry at Foxhole Level," may be misleading, since 80 per cent of the psychoneurotics in the army never were overseas and certainly never near a foxhole.

One might criticize the author on two points. The first is his almost benign attitude toward hospitals which returned a large percentage of psychoneurotics to full duty without regard to the men's welfare or that of their organizations, in order to have their record of "men returned to duty" high enough to get the C.O. his Legion of Merit. The other is his naive conclusion that certain 4-F's, such as athletes and crooners, were merely victims of publicity and were so classified only because they did not meet the minimum induction standards. This is extremely difficult to believe in view of the fact that combat infantrymen with old ear-drum perforations, marked hearing defects, and "trick" knees could not be relieved from front-line duty in spite of every effort by their surgeons.

This book will be of interest to the veteran doctor as well as to the non-veteran doctor interested in the psychoneurosis of soldiers. The story of the army's handling and mishandling of that problem is interestingly told in conversation which reads more like a novel than non-fiction. The various technical points of psychiatry are kept remarkably straight by the author's collaborators, who include W. C. Menninger, Brill, Strecker, and other well-known psychiatrists.

Book Catalogue

Chemical Publishing Co., Inc., 26 Court Street, Brooklyn 2, N. Y. has just issued their new 1947 catalog. The catalog includes the latest books on chemistry, technology, physics, general science, mathematics, engineering, foods, formularies, drugs and cosmetics, medicine, metals, technical dictionaries, etc., as well as college and other textbooks.

Librarians, technical and scientific workers will find this catalog especially useful as it conforms with many of their specific needs in listing the date of publication of each book, as well as price, number of pages, descriptions and full table of contents.

Keep up with the last developments in science and industry by writing direct to the publisher for a free copy of this catalog.

BULLETIN BOARD

(CONTINUED FROM PAGE 186)

American College of Chest Physicians

The Thirteenth Annual Meeting of the American College of Chest Physicians is scheduled to be held at the Ambassador Hotel, Atlantic City, New Jersey, June 5 to 8. An interesting scientific program has been planned for this meeting. Prominent speakers from other countries will present papers.

The oral and written examinations for Fellowship will be held on the first day of the meeting, June 5. Applicants for Fellowship in the College who plan to take these examinations should communicate at once with the Executive Secretary, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

The Convocation for new Fellows and Life Members of the College will be held on Sunday, June 8. At this time certificates will be awarded to Fellows and Life Members admitted since June, 1946.

American Society for Research in Psychosomatic Problems

The Fourth Annual Meeting of the American Society for Research in Psychosomatic Problems will take place on May 3 and 4, 1947, at Haddon Hall, Atlantic City. A morning and afternoon session are scheduled for Saturday, May 3, and the Annual Dinner will be held that evening. A panel discussion will be conducted Sunday morning.

The Society is particularly fortunate in having Dr. James L. Halliday of Scotland as one of its guest speakers. His research in psychosomatic medicine is well known, and his numerous articles have been published in medical journals here and abroad.

No registration fee will be required. Room reservations may be made directly through the hotel or the American Society for Research in Psychosomatic Problems, but dinner reservations must be made through the Society's office at 714 Madison Avenue, New York 21, New York.

National Mental Health Foundation

An expanded program of public education on the problems and needs of mental patients will be undertaken by the National Mental Health Foundation through grants of $25,000 each from Carnegie Corporation of New York and the Rockefeller Foundation, Harold Barton, executive secretary of the nonprofit mental health organization, announced recently.

Started in April, 1944, by a group of young volunteer attendants in a Pennsylvania state mental hospital, the Foundation has a three-point program: (1) to inform the public on the need for more progressive and humane treatment of mental cases; (2) to secure adequate mental health facilities in every state; and (3) to encourage better training for attendants in mental hospitals.

DOCTOR WANTED—The town of Waxhaw in Union County is without a doctor. A physician locating in Waxhaw would serve between 5000 and 6000 people and would have the facilities of the hospital in Monroe, twelve miles distant, at his disposal. Anyone interested in this location should write Mr. Robert Howie, Waxhaw, N. C.

American Foundation for Tropical Medicine

To encourage the study of tropical medicine and to stimulate research into new methods of treatment and control, the facilities of the new $250,000 Liberian Institute will be open to students and scientists of all lands without distinction as to color, race or creed. Its research findings will also be available to all who are interested.

Construction of the Institute's buildings, a gift from Harvey S. Firestone Jr., as a memorial to his late father, will be started this year on a 100-acre site adjoining Roberts Field, international airport of West Africa. This land, together with an additional 600 acres of choice farming land, is a tax-free gift from the Liberian Government, which has agreed to cooperate fully with the work of the Institute.

A campaign for $250,000 to cover the first year's operations is now in progress by the Foundation, whose offices are located at 270 Madison Avenue, New York 16, N. Y. Industries with an interest in tropical medicine and economy will be asked to support the work of the Institute, whose scientific program will be guided by a committee made up of representatives of seventeen universities, the army and navy medical services, the U. S. Public Health Service, and industries interested in the development of this phase of medicine. Included in this group are Dr. Thomas T. Mackie, representing the Bowman Gray School of Medicine, and Dr. Donald S. Martin, representing the Duke University School of Medicine.

Growth of Blue Cross in State and Nation

Over 55,000 North Carolinians were added to the membership rolls of the Hospital Saving Association during 1946, a record year for the organization. Enrollment in the state totals 315,000 members, now protected against hospital bills. Of this number, 180,000 are also protected against surgical claims. One out of every 11 North Carolinians is protected by the Chapel Hill Blue Cross Plan. Fifty per cent of the population of Winston-Salem is covered by the Association.

Blue Cross Hospital Service gained 5,887,219 new members in 1946 to establish an all-time enrollment record, Richard M. Jones, acting director, Blue Cross Commission, American Hospital Association, announced recently in Chicago. Membership increases in each quarter were greater than in any previous quarter in Blue Cross history. The highest gains on record were set in the second and fourth quarters, with enrollment of one and three fourths and one and one half million members, respectively.

In releasing the enrollment figures, Jones said, "Blue Cross growth for 1946 represented the enrollment of 45 members each working day minute. This phenomenal growth clearly demonstrates the success of voluntary methods in providing a means of prepayment for hospital care as protection against the financial hazards of unexpected illness. Total membership is now 25,876,424, indicating that one person in five is a Blue Cross member.

Sites now have been selected for 68 of the 75 new hospitals which Veterans Administration is authorized to build and for which funds have been appropriated.

Firecracker Victims

A survey conducted by the Hospital Care Association, a non-profit Blue Cross organization serving North Carolina, recently disclosed that more than 700 patients were treated for injuries resulting from fireworks in North Carolina during a thirty-day period. Seventy-four were admitted to hospitals; 16 lost the sight of one eye; many lost fingers; many were seriously burned. Two hundred and sixty-one physicians participated in the survey. Many additional cases were unreported.

A new Borden prescription product, Gerilac Modified Milk, is being introduced to the medical profession and drug trade in the North Carolina area, it has been announced by Borden Company officials.

Gerilac is a spray-dried mixture of whole milk, skim milk, dried brewer's yeast fortified with riboflavin concentrate, vitamins A and D concentrate, irradiated ergosterol, ascorbic acid, niacinamide, monosodium phosphate and iron citrate. It has been tested clinically at several homes for the aged and gave significant results. Plain, the product has a pleasing taste, and variety may be enjoyed by the addition of flavors such as vanilla and chocolate. It may be served either as a beverage or used in cooking and baking.

Gerilac is sold in drug stores in one pound cans.

Three new products are being introduced to doctors by the Winthrop Chemical Company, Inc., according to announcement made by J. G. Noh, vice-president and sales director. They are Digisidin, the principal glycoside of digitalis, known commonly as Digitoxin; Pluraxin, a therapeutic formula type of multi-vitamin product; and Pontocaine Neo-Synephrine 0.25 per cent solution, an anesthetic-vasoconstrictor for topical use.

Digisidin is supplied in tablets of 0.1 mg. (pink) and 0.2 mg. (white) in bottles of 50, 100 and 500.

The formula for Pluraxin is:

Vitamin A—25,000 U.S.P. units
Vitamin B_1—15 mg.
Vitamin B_2—10 mg.
Vitamin B_6— 2 mg.
Vitamin C—150 mg.
Vitamin D_2—1000 U.S.P. units
Calcium Pantothenate 10 mg.
Niacinamide 150 mg.

It is supplied in bottles of 30 capsules and 100 capsules.

Pontocaine Neo-Synephrine 0.25 per cent solution is supplied in 1-ounce and 8-ounce bottles.

For Shy, Nervous, Retarded Children

Year round private home and school for girls and boys of any age on pleasant 150 acre farm near Charlottesville.

Individual training and care, expert teachers. Limited enrollment, amusements, special diets, medical care if necessary. Entrance made at any time. Write for Booklet.

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